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VOL. 26, SEC. B.

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NUMBER 4

THE SULPHONATION OF CHLOROBENZENE¹

BY H. R. CHIN-YEE² AND C. A. WINKLER

Abstract

The rate of heterogeneous sulphonation of chlorobenzene in sulphuric acid solutions of different concentrations has been found to increase with amount and concentration of acid used, and with increase of temperature. No appreciable amount of sulphone was formed under the conditions used.

Introduction

Work in this laboratory (1) and elsewhere (3) indicates sulphonation of chlorobenzene to be a major factor contributing to unfavorable yields of 1,1-di(4-chlorophenyl)-2,2,2-trichloroethane (*p,p'*-D.D.T.) in the condensation of chlorobenzene with chloral (molar ratio 2 : 1), using concentrated sulphuric acid as catalyst. The main characteristics of the sulphonation reaction in sulphuric acid solutions of different concentrations have therefore been studied, and are outlined in the present paper.

Apparatus and Materials

The thermostat, maintained at constant temperature (within 0.1° C.), was fitted with a stirrer for each of six individual flasks whose corks were covered with lead foil. The stirrers were all driven at the same speed from a common shaft.

The reaction was followed by alkali titration of the residual sulphuric acid using a burette to which was sealed an accurately calibrated 125 ml. bulb to increase its capacity. Carbon dioxide was excluded from the burette and sodium hydroxide solution.

C.p. chlorobenzene was distilled and the fraction boiling between 131° and 132° C. was used in the experiments.

Sulphuric acid concentrations above 95% were obtained by adding oleum (20% SO₃) to 95% sulphuric acid.

¹ Manuscript received in original form July 25, 1947, and, as revised, January 19, 1948.

Contribution from the Physical Chemistry Laboratory, McGill University, Montreal, Que.

² Holder of a National Research Council bursary.

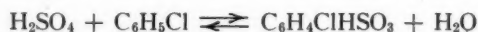
Procedure

Sulphuric acid (approximately 9 gm. quantities) was weighed directly into 50 ml. extraction flasks and allowed to come to the temperature of the thermostat, after which 2 ml. (2.208 gm.) of chlorobenzene was added to each flask, and the stirring started.

The reaction was stopped after the desired time intervals by placing the reaction vessel in dry ice - acetone mixture. After removing the reaction mixture from the dry ice - acetone, 30 gm. of chopped ice was added and the flask shaken vigorously for 30 sec.

The reaction mixture was poured immediately into a 500 ml. Erlenmeyer flask and the extraction flask washed three or four times with distilled water, the washings being collected in the Erlenmeyer flask. The mixture was titrated immediately with approximately 1 *N* sodium hydroxide solution, using phenolphthalein as indicator.

From the equation:



it can be seen that, if all the sulphuric acid reacts, the acidity of the medium drops to one-half its initial value (5, 7). That is:

$$(\text{Initial NaOH titer}) - (\text{Final NaOH titer}) = \text{Decrease in titer,}$$

and

$$\frac{\text{Decrease in titer} \times 2}{\text{Initial NaOH titer}} = \text{Fraction H}_2\text{SO}_4 \text{ reacted.}$$

The initial titer of sodium hydroxide required was calculated for the weighed amount of sulphuric acid in each flask, the alkali and acid used having been compared previously.

$$\text{Finally, \% chlorobenzene reacted} = \frac{\text{moles H}_2\text{SO}_4}{\text{moles C}_6\text{H}_5\text{Cl}} \times \% \text{ H}_2\text{SO}_4 \text{ reacted.}$$

In the heterogeneous reaction involving an acid layer and a chlorobenzene layer, the rate of stirring is an important factor. The rate of stirring was therefore increased until no change in the rate of the reaction was noted. A stirring speed in the order of 1400 r.p.m. was found to give data reproducible within $\pm 3\%$.

Results

In Tables I to IV and Fig. 1 are recorded the experimental data obtained at different temperatures with different molar ratios of chlorobenzene and sulphuric acid solutions of different strengths. The data of Fig. 1 were obtained by varying the amount of chlorobenzene with constant amount of sulphuric acid.

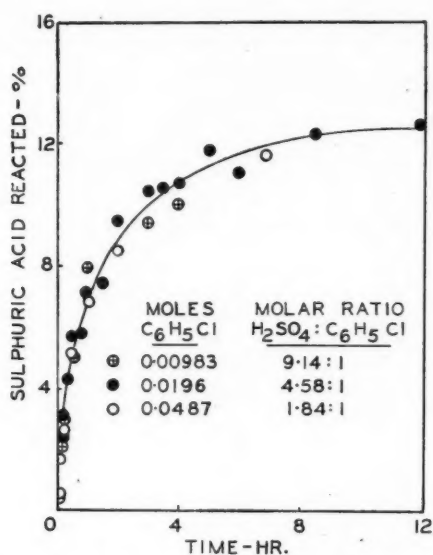


FIG. 1. The effect of chlorobenzene amounts on the rate of sulphonation. 98.4% sulphuric acid: 0.0898 mole. Temperature: 30° C.

TABLE I

RATE OF SULPHONATION OF CHLOROBENZENE WITH 93.5% SULPHURIC ACID

Initial amounts: Chlorobenzene: 0.0196 mole
Sulphuric acid: 0.0852 mole

Time, hr.	% Chlorobenzene reacted at temperatures of:			
	30° C.	45° C.	55° C.	67.5° C.
0.5	—	—	7.1	16.6
1.0	4.1	6.6	12.6	28.0
2.0	—	—	19.0	34.6
2.5	—	10.6	—	—
3.0	4.7	12.7	—	—
4.0	—	16.0	28.4	43.0
5.3	10.8	—	—	—
6.0	—	20.2	32.6	47.8
6.3	—	20.3	—	—
7.0	10.9	—	—	—
8.0	—	—	39.2	58.3
8.4	—	25.3	—	—
9.0	10.8	—	—	—

TABLE II

RATE OF SULPHONATION OF CHLOROBENZENE WITH 96.3% SULPHURIC ACID

Initial amounts: Chlorobenzene: 0.0196 mole

Sulphuric acid: 0.0879 mole

Time, hr.	% Chlorobenzene reacted at temperatures of:			
	20° C.	30° C.	45° C.	55° C.
0.1	—	—	5.1	—
0.25	—	—	—	21.2
0.50	—	—	20.6	29.6
1.0	5.38	11.1	25.8	35.0
1.5	—	—	—	46.2
2.0	7.7	19.4	36.8	53.4
4.0	13.3	30.8	44.2	60.0
6.0	17.9	36.5	53.4	66.0
7.0	—	36.4	—	—
7.5	19.7	—	—	—
8.0	—	—	55.6	66.8
9.0	21.4	38.6	—	—

TABLE III

RATE OF SULPHONATION OF CHLOROBENZENE WITH 98.4% SULPHURIC ACID

Initial amounts: Chlorobenzene: 0.0196 mole

Sulphuric acid: 0.0898 mole

Time, hr.	% Chlorobenzene reacted at temperatures of:			
	0° C.	20° C.	30° C.	45° C.
0.02	—	—	5.2	7.0
0.10	—	—	12.3	26.4
0.25	—	4.9	14.5	31.8
0.32	—	—	19.6	40.5
0.50	—	—	26.0	43.8
0.75	—	—	26.4	—
1.00	—	14.5	32.8	48.6
1.5	3.2	—	34.2	—
2.0	—	23.9	43.4	61.0
3.0	5.8	—	47.7	72.5
4.0	—	33.6	49.0	—
5.0	—	—	54.1	78.6
6.0	9.5	34.0	50.8	—
9.0	11.2	—	—	—
12.0	14.2	—	57.9	—

TABLE IV

RATE OF SULPHONATION OF CHLOROBENZENE WITH 101% SULPHURIC ACID

Initial amounts: Chlorobenzene: 0.0196 mole
Sulphuric acid: 0.0923 mole

Time, hr.	% Chlorobenzene reacted at temperatures of:			
	0° C.	20° C.	30° C.	45° C.
0.03	26.9	35.6	44.6	49.5
0.25	33.1	47.0	61.1	70.1
0.58	—	54.6	—	—
0.63	37.5	—	—	—
0.68	—	—	71.5	—
0.82	—	—	—	91.8
1.0	39.8	59.2	75.7	—
1.5	—	—	80.0	96.0
2.0	44.8	67.3	—	—
2.5	—	—	86.6	—
3.0	47.5	73.5	—	97.0
3.5	—	—	91.4	—
4.0	49.9	—	75.2	97.0
4.5	—	—	92.2	—
5.0	52.2	80.0	—	—
5.8	53.2	—	94.1	—

Discussion

With given amount of sulphuric acid, the rate of acid consumption (corresponding to moles chlorobenzene reacted) is substantially the same for different amounts of chlorobenzene present, at least over the range of mole ratios studied (Fig. 1). This implies that reaction occurs between the sulphuric acid and chlorobenzene dissolved in it. Hence, if the quantity of sulphuric acid were increased, other conditions remaining unaltered, the amount of chlorobenzene reacting per minute should increase, although the amount reacting per minute per mole of acid should not be affected.

The marked decrease in rate of sulphonation with decrease of acid concentration (Fig. 2) probably reflects an increased tendency for the reverse hydrolytic reaction (6), together with decreased solubility of chlorobenzene, in acids of higher water contents.

Comparison of the rate curves for acids below 100% with those for 101% acid (Fig. 3) shows a marked difference. The curves for 101% acid are characterized by a rapid reaction initially, followed by slower reaction. The behavior may be rather simply explained if it is assumed that SO_3 (or perhaps S_2O_6 or $\text{S}_2\text{O}_7^{2-}$) is responsible for most of the sulphonation in acids above 100% (2, 8) and that the subsequent slower reaction may be attributed to sulphuric acid after the SO_3 has been consumed. In fact, the rate of the slower reaction corresponds to that for an acid of approximately 99% concentration.

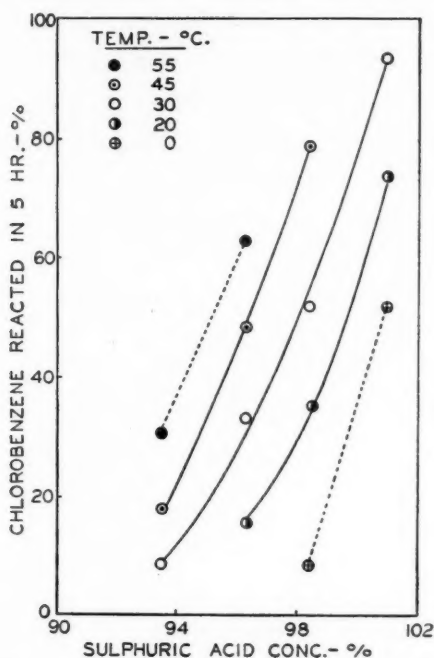


FIG. 2. The effect of sulphuric acid concentration on the amount of chlorobenzene reacted in five hours at various temperatures. Molar ratio: 5:1.

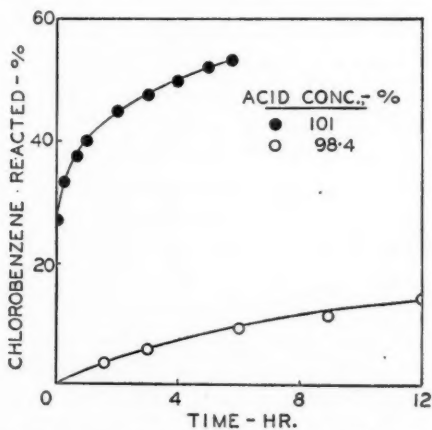


FIG. 3. Typical rate curves for acids above and below 100%. Temperature: 0°C.

Although chlorobenzene and chlorosulphonic acid may be condensed in fuming sulphuric acid to yield a sulphone (4), there was no indication that sulphone formation occurred in the present study with 101% acid. If sulphone

were formed, an induction period in the rate curves would be expected, since the formation of sulphone should decrease the acidity twice as much as the formation of chlorosulphonic acid. Moreover, the (4-chlorophenyl) sulphone is water insoluble and no water insoluble material other than unreacted chlorobenzene remained in the reaction vessels after titration. The possibility that the sulphone remained dissolved in unreacted chlorobenzene may be ruled out, since no water insoluble product separated even after 97% reaction of the chlorobenzene.

A marked dependence of the rate of the sulphonation reaction on temperature is illustrated in Fig. 4. Change of temperature undoubtedly alters factors other than reaction rate itself, for example, the solubility of chlorobenzene in the acid, so that an activation energy for the reaction cannot be obtained from the data.

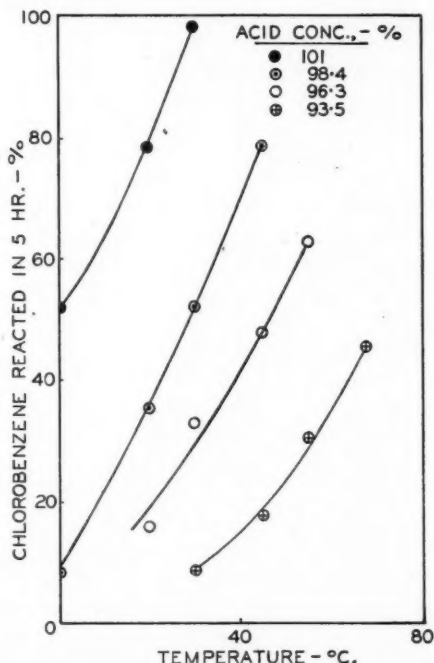


FIG. 4. The effect of temperature on the amount of chlorobenzene reacted in five hours at various sulphuric acid concentrations.

The relation of the present study to the DDT reaction (1) might be briefly indicated. In the DDT reaction, chlorobenzene will be consumed by both the condensation and sulphonation reactions. Maximum yield of DDT will be possible, therefore, only if an amount of chlorobenzene is present initially in excess of that consumed by both reactions. The *rate* of DDT formation will be decreased owing to a fall in acid concentration as sulphonation proceeds.

The use of sulphuric acid in concentrations above 100% in the DDT reaction would seem to have no advantage, not only because sulphone is formed under such conditions (1), but also because the initial rate of the sulphonation reaction is high, even at low temperatures.

Since the rate of sulphonation of chlorobenzene is favored by an increase of temperature, low temperatures should favor the yield of DDT.

References

1. EASTWOOD, T. A., GARMAISE, D. L., MORANTZ, D. J. and WINKLER, C. A. *Can. J. Research*, B, 25 : 509. 1947.
2. MICHAEL, A. and WEINER, N. *J. Am. Chem. Soc.* 58 : 294. 1936.
3. MOSHER, H. S., CANNON, M. R., CONROY, E. A., VAN STRIEN, R. E., and SPALDING, D. P. *J. Ind. Eng. Chem.* 38 : 916. 1946.
4. OTTO, R. *Ann.* 145 : 28. 1868.
5. SIMPSON, W. A. and OLSEN, J. C. *J. Ind. Eng. Chem.* 29 : 1350. 1937.
6. SPRYSKOV, A. A. *J. Gen. Chem. U.S.S.R.* 8 : 1857. 1938.
7. VICARY, D. R. and HINSHELWOOD, C. N. *J. Chem. Soc.* 1372. 1939.
8. WADSWORTH, K. D. and HINSHELWOOD, C. N. *J. Chem. Soc.* 469. 1944.

THE SYNTHESIS OF D,L- α -AMINO- ϵ -HYDROXYCAPROIC ACID AND A NEW SYNTHESIS OF D,L-LYSINE¹

BY ROGER GAUDRY

Abstract

δ -Hydroxyvaleraldehyde, obtained by acid hydrolysis of dihydropyran, is a convenient starting material for the synthesis of D,L-lysine. Application to the aldehyde of the Bucherer modification of the Strecker synthesis for α -amino acids yields 5- δ -hydroxybutylhydantoin which is hydrolyzed into D,L- α -amino- ϵ -hydroxycaproic acid. D,L-Lysine is obtained from 5- δ -hydroxybutylhydantoin by bromination with hydrobromic acid into 5- δ -bromobutylhydantoin, amination of the bromo compound with ammonia, and hydrolysis of the hydantoin ring into D,L-lysine, readily isolated as the dipicrate.

Introduction

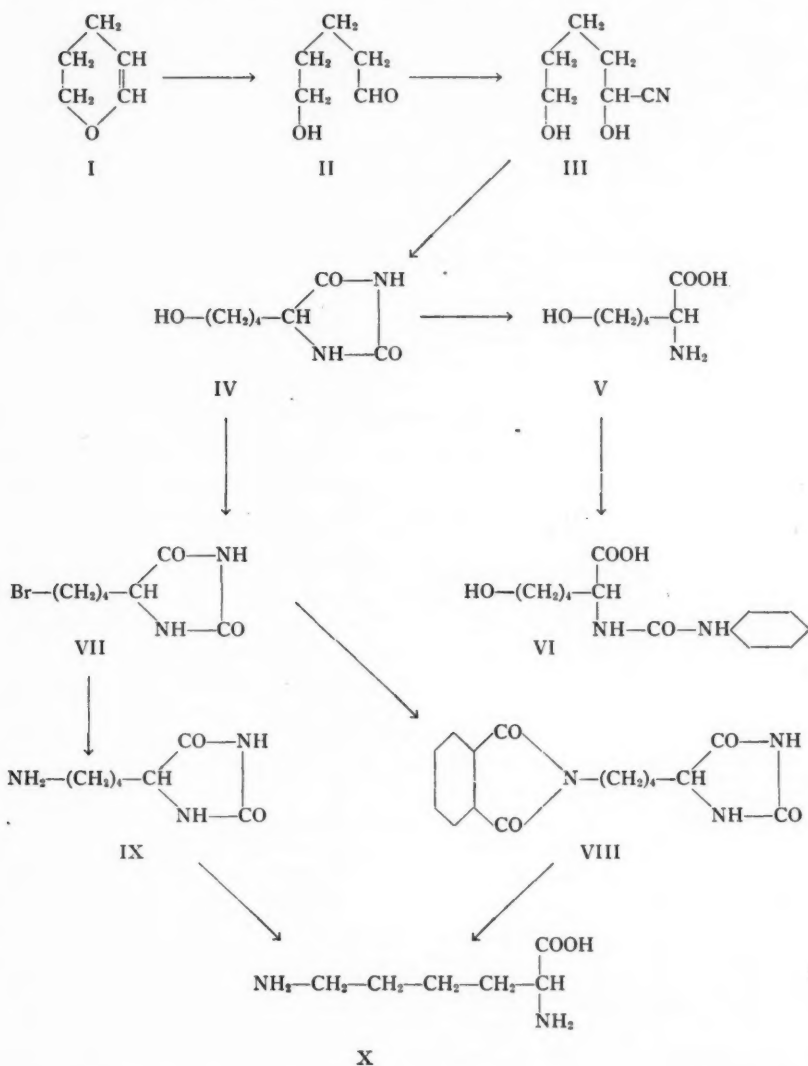
Many syntheses of D,L-lysine (X) have been published (14), but only the von Braun method (4), improved by Eck and Marvel (6) and recently modified by Galat (8) seems to have any application. The easy preparation of δ -hydroxyvaleraldehyde (II) from the now available dihydropyran (I) (15) suggested to us the possibility of synthesizing lysine (X) from dihydropyran (I). δ -Hydroxyvaleraldehyde (II), prepared by the method of Schniepp and Geller (15), was not isolated but its aqueous solution was used directly to prepare the bisulphite addition compound and the corresponding cyanohydrin, α , ϵ -dihydroxycaproic nitrile (III). Most of the nitrile separates as an oil from the aqueous solution, while the rest is extracted with a large volume of ether, in which it is not very soluble. Heating the α , ϵ -dihydroxycaproic nitrile (III) with an excess of ammonium carbonate according to Bucherer and Lieb (5) gives 5- δ -hydroxybutylhydantoin (IV) in a 73.3% over-all yield from dihydropyran (I). Hydrolysis of this hydantoin with barium hydroxide under pressure gives a 95% yield of D,L- α -amino- ϵ -hydroxycaproic acid (V), which is of interest because it is probably identical with the anemia producing factor* of deaminized casein.

Fischer and Tiemann (7), and later Neuberg, Wolff, and Neimann (13) have prepared by reduction of glucosaminic acid a compound that gave analytical figures corresponding to $C_6H_{13}O_3N$. Levene and coworkers (11, 12) also prepared by reduction of chondrosaminic acid a compound that is an amino-hydroxycaproic acid. But to our knowledge, α -amino- ϵ -hydroxycaproic acid has never been previously prepared by a method that establishes its chemical structure.

¹ Manuscript received December 16, 1947.

Contribution from the Department of Biochemistry of the Faculty of Medicine, Laval University, Quebec, Que.

* The results of biological investigations on the anemia producing properties of that compound will be published elsewhere. Since it is a serine homologue and a six carbon compound, it is proposed that it be called 'hexahomoserine'.



5- δ -Hydroxybutylhydantoin (IV), by treatment with 48% hydrobromic acid, gives an 80% yield of 5- δ -bromobutylhydantoin (VII). 5- δ -Chlorobutylhydantoin is also obtained by treatment with thionyl chloride, but in a much lower yield. Heating the bromo compound with potassium phthalimide gives 5- δ -phthalimidobutylhydantoin (VIII), a lysine derivative which gives lysine by acid hydrolysis followed by alkaline hydrolysis. 5- δ -Bromobutylhydantoin (VII) is aminated in presence of an excess of ammonia to give

5- δ -aminobutylhydantoin (IX) (9), the hydrochloride of which is very difficult to recrystallize. Its picrate is readily obtained in a crystalline form, but its analysis corresponds to that of the monohydrate. There is no doubt however that the compound is the hydantoin monohydrate, and not the corresponding hydantoic acid, for it gives the characteristic color reaction of hydantoins (2,3) which is not given by hydantoic acids; other 5-substituted hydantoins are also known to give very stable hydrates (10). Alkaline hydrolysis of 5- δ -aminobutylhydantoin (IX) gives D,L-lysine (X), which is readily precipitated from its aqueous solution as the dipicrate, in a 54.6% yield from 5- δ -hydroxybutylhydantoin (IV), or a 40% over-all yield from dihydropyran (I). It may be pointed out that all the reactions are carried out in aqueous solution, and all the compounds that have to be isolated in the course of this synthesis of lysine are readily recrystallized from water.

It is expected that these reactions, applied to dihydrofuran instead of dihydropyran, will yield D,L-ornithine in the same way.

Experimental

5- δ -Hydroxybutylhydantoin (IV)

Dihydropyran (100 gm., 1.19 moles) was hydrolyzed to δ -hydroxyvaleraldehyde with 0.02 *N* hydrochloric acid as described by Schniepp and Geller (15). After carefully neutralizing the solution with sodium hydroxide, dry sodium acid sulphite (125 gm., 1.20 moles) was added with good mechanical stirring to the aqueous solution of the aldehyde kept at room temperature by dipping the flask into a bath of cold running water. When all the sodium bisulphite had dissolved, a solution of potassium cyanide (78 gm., 1.2 moles) in water (100 ml.) was slowly added, and stirring was continued at room temperature for two hours. The mixture was poured into a separatory funnel, the upper layer was separated, and the aqueous layer was extracted four times with large volumes (4×250 ml.) of ether. The ether was evaporated on the water bath, and the residue was added to the main portion from the upper layer. This liquid, which is nearly pure, colorless α , ϵ -dihydroxycaproic nitrile, was added to a solution of ammonium carbonate (230 gm., 2.4 moles) in water (400 ml.) and the mixture was stirred for one hour while being kept at 50° to 55° C. in a water bath. The temperature of the bath was then raised slowly to boiling, a little Norit added, and the solution was filtered into a large evaporating dish and evaporated to dryness on a water bath. The residue was recrystallized from water; m.p. 152° to 155° C.* Yield, 151 gm., 73.3%. Calc. for $C_7H_{12}O_3N_2$: N, 16.27%. Found (Kjeldahl): N, 16.17%.

D,L- α -Amino- ϵ -hydroxycaproic acid (V)

5- δ -Hydroxybutylhydantoin (51.6 gm., 0.30 mole) and barium hydroxide (151.5 gm. of the octahydrate, 0.48 mole) were mixed together in boiling water (750 ml.) and the solution was heated in an autoclave at 160° C. for

* Melting points are uncorrected.

half an hour. The solution was cooled, filtered from the barium carbonate, treated with powdered ammonium carbonate (30 gm.), again filtered from the barium carbonate, and evaporated to dryness under reduced pressure. The residue was slurried with methanol and filtered to give pure D,L- α -amino- ϵ -hydroxycaproic acid. It is readily recrystallized from water. Yield, 41.5 gm., 95%. The melting point varies between 245° and 248° C. and 260° and 262° C. with evolution of gas, according to the rate of heating. Calc. for $C_6H_{13}O_3N$: N, 9.52%. Found (Kjeldahl): N, 9.45%. The picrate melts at 127° to 130° C. Calc. for $C_{12}H_{18}O_{10}N_4$: N, 14.89%. Found: N, 14.56%.

D,L- α -Phenylureido- ϵ -hydroxycaproic Acid (VI)

D,L- α -Amino- ϵ -hydroxycaproic acid (1 gm.) was dissolved in one equivalent of dilute aqueous sodium hydroxide solution. On shaking strongly for a few minutes with one equivalent of phenylisocyanate, the mixture became warm. It was cooled, filtered, and acidified with dilute hydrochloric acid. The precipitate rapidly crystallized on standing in the ice box. It was recrystallized from aqueous alcohol. Yield, 1.2 gm., 66%. It melts at 141° C. with evolution of gas. Calc. for $C_{13}H_{18}O_4N_2$: N, 10.52%. Found (Kjeldahl): N, 10.50%.

5- δ -Bromobutylhydantoin (VII)

5- δ -Hydroxybutylhydantoin (34.4 gm., 0.2 mole) was treated with 48% hydrobromic acid (400 ml.), and the solution was kept at 90° C. for two hours, in a water bath. It was then evaporated to dryness *in vacuo*; the residue was dissolved in boiling water (300 ml.), boiled under reflux for five minutes with a little Norit, filtered, and allowed to cool. The precipitate was filtered and the solution was evaporated to dryness *in vacuo*. The residue was again treated with 48% hydrobromic acid (100 ml.) for two hours at 90° C., the acid was evaporated *in vacuo*, and the residue decolorized with Norit and crystallized from hot water (30 ml.). Total yield: 38.8 gm., 80%. After two crystallizations, the melting point was 129° to 131° C. Calc. for $C_7H_{11}O_2N_2Br$: N, 11.97%. Found (Kjeldahl): N, 11.91%.

5- δ -Chlorobutylhydantoin

5- δ -Hydroxybutylhydantoin (17.2 gm., 0.1 mole) and thionyl chloride (7.6 gm., 0.1 mole) were rapidly mixed in a beaker with a glass rod, and allowed to stand for one hour at room temperature, under a hood. The mixture was then dissolved in hot water (100 ml.) and cooled. The precipitate was filtered and recrystallized from a little hot water. Yield, 4.0 gm., 21%. Melting point, 126° to 128° C. Calc. for $C_7H_{11}O_2N_2Cl$: N, 14.70%. Found (Kjeldahl): N, 14.66%.

5- δ -Phthalimidobutylhydantoin (VIII)

5- δ -Bromobutylhydantoin (23.5 gm., 0.1 mole) and potassium phthalimide (18.5 gm., 0.1 mole) were intimately mixed in a mortar; the mixture was transferred to a conical flask and heated at 150° C. for one and a half hours

in an oil bath. After cooling, the mass was washed in the mortar by decantation with three portions of water (100 ml.) and recrystallized from a mixture of water (225 ml.) and alcohol (150 ml.). A yield of 18.3 gm. was obtained, which was raised to 24.0 gm. (80%) by working up the mother liquor. After three crystallizations, the melting point was 212° to 215° C., with sintering at about 170° C. Calc. for $C_{15}H_{15}O_4N_3$: N, 13.95%. Found (Kjeldahl): N, 13.93%.

5- δ -Aminobutylhydantoin (IX)

5- δ -Bromobutylhydantoin (7.83 gm., 0.033 mole) and concentrated ammonia (160 ml.) were placed in a 200 ml. pressure bottle, and the solution was heated at 60° C. for four days. The solution was evaporated to dryness *in vacuo*. The residue was dissolved in water (100 ml.); the solution was boiled for a few minutes with freshly precipitated silver oxide (4 gm.), filtered, acidified with a slight excess of hydrochloric acid, and evaporated to dryness *in vacuo*. 5- δ -Aminobutylhydantoin hydrochloride slowly solidified on standing. It is very soluble in water and alcohol, and precipitates as an oil by adding ether to the alcoholic solution. It was not obtained in a pure state, but only as pale brownish powder that melted at 163° to 170° C. Calc. for $C_7H_{14}O_2N_3Cl$: N, 20.24%. Found (Kjeldahl): N, 19.25%.

The picrate was obtained by treating the aqueous solution of the hydrochloride with one equivalent of picric acid, and was recrystallized from very little water. Melting point, 180° to 183° C. Its analysis corresponds to that of the monohydrate. Calc. for $C_{13}H_{16}O_9N_6 \cdot H_2O$: N, 20.09%. Found: N, 20.01%.

D,L-Lysine (X)

5- δ -Bromobutylhydantoin (23.5 gm., 0.1 mole) was aminated in the presence of a large excess of concentrated ammonia (500 ml.) by heating for four days at 60° C. in pressure bottles. The solution was evaporated to dryness under reduced pressure. The residue was dissolved in a solution of barium hydroxide (78 gm., 0.25 mole of the octahydrate) in hot water (500 ml.), and heated in an autoclave at 160° C. for one-half hour. After cooling, the mixture was filtered, and the solution treated with an excess of ammonium carbonate (30 gm.), filtered again from the barium carbonate, and evaporated to dryness *in vacuo*. The residue was acidified with an excess of dilute hydrochloric acid and evaporated to dryness. The mixture of crude lysine dihydrochloride and ammonium bromide was dissolved in a solution of picric acid (23 gm.) in boiling water (1200 ml.). The solution was allowed to cool, and placed in the ice box for 48 hr. Lysine dipicrate (26.0 gm., 68.5%) crystallized out. A sample, which was recrystallized from a little hot water, melted at 188° C. The melting point was not depressed when the sample was mixed with an authentic one. Adamson (1) gives 188° to 190° C. as the melting point.

Pure D,L-lysine dihydrochloride was readily obtained from the dipicrate, in an 88% yield, by treating the dipicrate with an excess of aqueous hydrochloric acid, filtering and extracting the last traces of picric acid with ether, decolorizing with Norit and evaporating to dryness *in vacuo*. The product obtained was the dihydrate, which melted at 186° to 189° C. after grinding with alcohol, filtering, and drying it at room temperature. Calc. for $C_6H_{16}O_2N_2Cl_2 \cdot 2H_2O$: N, 10.98%. Found (Kjeldahl): N, 10.91%.

Acknowledgments

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References

1. ADAMSON, D. W. J. Chem. Soc. 1564. 1939.
2. BERNHEIM, F. and BERNHEIM, M. L. C. J. Biol. Chem. 163 : 683. 1946.
3. BONSNES, R. W. and TAUSKY, H. H. J. Biol. Chem. 158 : 581. 1945.
4. BRAUN, J. VON. Ber. 42 : 839. 1909.
5. BUCHERER, H. T. and LIEB, V. A. J. prakt. Chem. 141 : 5. 1934.
6. ECK, J. C. and MARVEL, C. S. Org. Syntheses 19 : 18; 20; 61. 1939.
7. FISCHER, E. and TIEMANN, F. Ber. 27 : 138. 1894.
8. GALAT, A. J. Am. Chem. Soc. 69 : 86. 1947.
9. HOPPE-SEYLER, F. A. Z. physiol. Chem. 214 : 267. 1932.
10. KLOSTERMAN, H. J. and PAINTER, E. P. J. Am. Chem. Soc. 69 : 2009. 1947.
11. LEVENE, P. A. and CHRISTMAN, C. C. J. Biol. Chem. 123 : 83. 1938.
12. LEVENE, P. A. and LA FORGE, F. B. J. Biol. Chem. 20 : 433. 1915.
13. NEUBERG, C., WOLFF, H., and NEIMANN, W. Ber. 35 : 4009. 1902.
14. SCHMIDT, C. L. A., *Editor*. The chemistry of the amino acids and proteins. 2nd ed. Charles C Thomas, Baltimore. 1944.
15. SCHNIEPP, L. E. and GELLER, H. H. J. Am. Chem. Soc. 68 : 1646. 1946.

THE SYNTHESIS OF L- α -GUAIACYL GLYCEROL ETHER¹

BY HERMANN O. L. FISCHER AND ALAN G. NEWCOMBE²

Abstract

The synthesis of L- α -guaiacyl glycerol ether is described.

Introduction

Recently it was discovered that D,L- α -guaiacyl glycerol ether, a well known expectorant, exerts an anaesthetic action on mice (5). Since enantiomers frequently display varying biochemical properties, it was, therefore, of interest to determine if the pharmacological properties of the L- and D,L-forms differed in any respect. For this purpose the synthesis of L- α -guaiacyl glycerol ether was undertaken.

L- α -Guaiacyl glycerol ether was prepared according to the following sequence of reactions: D-acetone glycerol (2) was converted to tosyl D-acetone glycerol (1), which was reacted with the sodium salt of guaicol, according to the method of Grosheintz (3), for the preparation of α -phenyl glycerol ether, to give α -guaiacyl D-acetone glycerol ether. Acid hydrolysis of the latter compound yielded L- α -guaiacyl glycerol ether.*

D,L- α -Guaiacyl glycerol ether was made by the method described above, with D,L-acetone glycerol as starting material. No change in the melting point was observed when the ether was mixed with commercially available material.

Experimental

D-Acetone Glycerol

D-Acetone glycerol was prepared according to the simplified procedure of Fischer and Baer (2).† The catalytic hydrogenation was, however, carried out at normal pressure using Raney nickel catalyst. The yield was 62%. $n_D^{22.5} = 1.4335$. Optical rotation: $[\alpha]_D^{22.5} = +13.92$. Reported by Fischer and Baer: $n_D^{20} = 1.4347$. Optical rotation: $[\alpha]_D^{20} = +13.98$.

Tosyl D-Acetone Glycerol

Tosyl D-acetone glycerol was prepared according to the method of Baer and Fischer (1). It was obtained in a crude yield of 96% and was used immediately without purification.

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Contribution from the Department of Chemistry, University of Toronto, Toronto, Ont. This paper forms part of a thesis submitted by A. Newcombe to the Department of Chemistry of the University of Toronto, in partial fulfillment of the requirements for the degree of Master of Arts, February, 1947.

² Recipient of a grant from the Banting Research Foundation, 1946.

* For details of the nomenclature and configuration of this type of compound see Fischer, H. O. L., and Baer, E. *Chem. Revs.* 29 : 295, 300. 1941.

† A detailed description, by E. Baer, of the most recent procedure for the preparation of D-acetone glycerol will appear in "Biochemical Preparations" as a part of the preparation of L- α -glycerophosphoric acid.

α -Guaiacyl D-Acetone Glycerol Ether

A mixture of 3.02 gm. (0.1312 mole) of sodium metal and 50 cc. of 99% alcohol was allowed to react in an open pressure vessel until all the sodium had disappeared; then 16.30 gm. (0.1312 mole) of guaiacol, 37.6 gm. (0.1312 mole) of tosyl D-acetone glycerol and 80 cc. of 99% alcohol were added. The flask was sealed, shaken at 60° C. until all the reactants had gone into solution, and then heated for two hours in an oven at 120° C. During the heating process the solution became dark red and after one hour a precipitate began to form. At the end of two hours the flask was allowed to cool to room temperature, and the precipitate, mainly the sodium salt of *p*-toluenesulphonic acid, was filtered off and washed with alcohol.

The filtrate was evaporated *in vacuo* to dryness, the residue was dissolved in water, and the aqueous solution was extracted 10 times with 50 cc. portions of ether. Some product was recovered by dissolving the sodium salt of *p*-toluenesulphonic acid in 100 cc. of water and extracting with ether. The combined ether extracts were washed twice with 100 cc. of 4 *N* sodium hydroxide solution, thrice with 100 cc. of water, and then dried over anhydrous sodium sulphate.

The ethereal solution was then concentrated to dryness *in vacuo* and the brownish residue dissolved in alcohol and decolorized with activated carbon. Upon slow evaporation of the alcohol, pure, white crystals of α -guaiacyl D-acetone glycerol ether precipitated. After air drying, the product weighed 17.5 gm. (55.7%); m.p. 47.0° to 49.0° C. For purposes of analysis and for the determination of optical activity the product was dried *in vacuo*. Optical rotation: $[\alpha]_D^{23} = +32.2$ ($c = 5.21$ in anhydrous benzene). Calc. for $C_{13}H_{18}O_4$ (238.3): C, 65.53; H, 7.61%. Found: C, 65.25; H, 7.54%.

 α -Guaiacyl D,L-Acetone Glycerol Ether

α -Guaiacyl D,L-acetone glycerol ether was made by the method above, using, however, tosyl D,L-acetone glycerol as starting material, which was prepared from D,L-acetone glycerol (4). The ether had a melting point of 47.5° to 49.5° C.

L- α -Guaiacyl Glycerol Ether

An amount of 17.4 gm. of α -guaiacyl D-acetone glycerol ether, together with 250 cc. of 12% acetic acid, was heated on a steam bath until all the crystals had gone into solution (approximately four hours). This solution was brought to dryness *in vacuo*. In order to remove any acetyl groups that may have entered the molecule, the residue was dissolved in water, and sodium hydroxide solution was added dropwise until the solution was alkaline to phenolphthalein. The solution was heated on a steam bath for an hour, with further addition of alkali as required, neutralized with dilute hydrochloric acid, and evaporated to dryness *in vacuo*. The residue was dissolved in hot benzene, filtered, and petrol ether (b.p. 35° to 60° C.) added until turbidity was permanent. The mixture was allowed to cool to room temperature and the

crystals filtered off and dried *in vacuo*. Pure L- α -guaiacyl glycerol ether was thus obtained in a yield of 9.10 gm. (69.2% based on the acetone compound). The over-all yield based on the D-acetone glycerol was 33.5%; m.p. 95.0° to 97.0° C. Optical rotation: $[\alpha]_D^{23.5} = -15.4$ ($c = 4.08$ in 95% alcohol). Calc. for $C_{10}H_{14}O_4$ (198.2): C, 60.60; H, 7.12%. Found: C, 60.67; H, 7.57%.

Acknowledgments

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References

1. BAER, E. and FISCHER, H. O. L. J. Am. Chem. Soc. 70: 609. 1948.
2. BAER, E. and FISCHER, H. O. L. J. Biol. Chem. 128: 463. 1939.
3. GROSHEINTZ, J. M. Dissertation, Zürich. E.T.H. 1937.
4. NEWMAN, M. S. and RENOLL, M. J. Am. Chem. Soc. 67: 1621. 1945.
5. SMITH, H. W. J. Pharmacol. 91: 93. 1947.

THE SYNTHESIS OF POSSIBLE DEGRADATION PRODUCTS OF MORPHINE AND METATHEBAINONE. IV.¹

BY H. L. HOLMES AND J. L. STOIK

Abstract

The observation of Holmes and Mann that bromine is eliminated during the condensation of amyl and ethyl formate with ethyl γ -(2-bromo-4,5-dimethoxyphenyl)-butyrate, when sodium ethylate is the condensing agent, has led to the substitution of chlorine for bromine in the above product in the hope that it might withstand the conditions of the reaction. These expectations were not realized and the required dienophile (5-chloro-7,8-dimethoxy-3,4-dihydro-2-naphthoic acid) was not available by this method for combination with 2-ethoxybutadiene-1,3 as a route to possible degradation products of metathebainone. The 5-chloro-7,8-dimethoxy-3,4-dihydro-1-naphthoic acid has been prepared and the methyl ester added to 2-ethoxybutadiene. The enol ethyl ether of the resulting adduct was readily hydrolyzed in dilute mineral acid and the keto-ester characterized as its oxime and dinitrophenylhydrazone.

Introduction

In Part III of this series (3) it has been established that the addition of 2-ethoxybutadiene-1,3 to methyl 3,4-dihydro-1-naphthoate followed by acid hydrolysis of the enol ethyl ether of the adduct yields methyl 7-keto-octahydrophenanthrene-13-carboxylate rather than the desired 6-keto isomer. In accordance with the electronic interpretation of the Diels-Alder reaction as advanced by Hudson and Robinson (5) it is to be expected that methyl 1-bromo-3,4-dimethoxy-6-keto-octahydrophenanthrene-14-carboxylate would result from the addition of the above diene to methyl 5-bromo-7,8-dimethoxy-3,4-dihydro-2-naphthoate and subsequent hydrolysis of the enol ether of the adduct. Attempts to prepare the above dienophile by the method of Holmes and Trevo (4) failed, since during the condensation of amyl or ethyl formate with ethyl γ -(2-bromo-4,5-dimethoxyphenyl)-butyrate the halogen was eliminated.

By replacement of the bromine by a chlorine atom it was hoped that the elimination of the halogen during the condensation might be circumvented (7). This was not realized since cyclization was accompanied by dehydrogenation with the formation of 6,7-dimethoxy-2-naphthoic acid (3). However, elimination of the chlorine atom from ethyl γ -(2-chloro-4,5-dimethoxyphenyl)-butyrate did not occur during the condensation of this ester with ethyl oxalate (1, 3) since hydrolysis of the resulting glyoxylic ester in 18% sulphuric acid and cyclization of the α -keto- δ -(2-chloro-4,5-dimethoxyphenyl)-valeric acid gave 5-chloro-7,8-dimethoxy-3,4-dihydro-1-naphthoic acid. In analogy with previous work (3) the adduct (12% yield) from the condensation of the methyl ester of this acid with 2-ethoxybutadiene-1,3 is considered to be methyl

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Contribution from the Department of Chemistry, University of Saskatchewan, Saskatoon, Sask., with financial assistance from the National Research Council of Canada; based on a thesis submitted by J. L. Stoik to the College of Engineering in partial fulfillment of the requirements for the degree of Bachelor of Science in Chemical Engineering.

1-chloro-3,4-dimethoxy-7-ethoxyhexahydrophenanthrene-13-carboxylate. The corresponding keto-ester resulted from the acid hydrolysis of this enol ether adduct and was characterized as its oxime and 2,4-dinitrophenylhydrazone. The keto-ester also condensed with two moles of amyl nitrite to give a diisomeric nitroso derivative.

Experimental*

γ -(2-Chloro-4,5-dimethoxyphenyl)-butyric acid

β -Veratroylpropionic acid (m.p. 153° to 157° C.) was prepared from veratrole and succinic anhydride in 81% yield (4). The Clemmensen reduction of this crude product afforded a 70 to 75% yield of *γ -veratrylbutyric acid*, b.p. 180° to 184° C. (2.5 mm.). The distillate soon solidified in the receiver.

The conditions for the preparation of *γ -(2-chloro-4,5-dimethoxyphenyl)-butyric acid* (2) must be adhered to rigorously or a dichloro-acid results. The dichloro-acid resulted when 11.0 gm. of *γ -veratrylbutyric acid* in 65 cc. of glacial acetic acid was cooled to 7° C. and vigorously stirred as a slow stream of chlorine, diluted with air, was bubbled into the solution for five hours. The yellow solution was poured into ice and water and the solid that separated was collected on a Büchner funnel. The acid was dissolved in sodium bicarbonate solution and decolorized with sodium sulphite and Norit. The clear filtrate was cooled and acidified with sulphuric acid, filtered, and dried. The yield of acid melting at 110° to 116° C. was 10.0 gm. (70%). This acid was further purified by conversion to the ethyl ester, b.p. 189° to 193° C. (2.5 mm.) and $n_D^{25} = 1.5308$, followed by saponification of the ester and crystallization of the acid from ether. The pure acid crystallized in flaky crystals and melted at 128° to 129° C. Neutral equivalent: Calc. for $C_{12}H_{14}O_4Cl_2$: 293.0. Found, 296.0.

The monochloro-acid was prepared by generating the theoretical amount of chlorine from 16.0 gm. of potassium permanganate and 104 cc. of concentrated hydrochloric acid. The dry chlorine (generated over a period of 70 min.) was diluted with a stream of air before passing it into a well stirred and cooled (+7° C.) solution of 44.0 gm. of the *γ -phenylbutyric acid* in 120 cc. of glacial acetic acid. When all the chlorine had been swept through the reaction flask the reaction mixture was poured into ice and water containing some sodium sulphite. The solid acid was collected on a Büchner funnel and air dried. The crude acid was triturated with ice-cold ether, whereupon 36.5 gm. (72.5%) of the insoluble *γ -(2-chloro-4,5-dimethoxyphenyl)-butyric acid* (m.p. 105° to 106° C.) was recovered. After two crystallizations from ether the acid melted at 110.5° to 112.0° C.

The ethyl ester (b.p. 169° to 173° C. (2.5 mm.) and $n_D^{25} = 1.5215$) was obtained in 91.5% yield upon esterification by the Fischer-Speier method.

* All melting points were taken in an apparatus designed by E. B. Hershberg, Ind. Eng. Chem., Anal. Ed. 8: 312, 1936, and are corrected. All compounds were analyzed in the analytical laboratories of Dr. Léo Marion, National Research Council, Ottawa, Canada, and Mr. A. Ledingham, Dominion Rubber Research Laboratory, Guelph, Ontario.

5-Chloro-7,8-dimethoxy-3,4-dihydro-1-naphthoic acid

α -Keto- δ -(2-chloro-4,5-dimethoxyphenyl)-valeric acid was prepared by condensing 57.2 gm. of ethyl γ -(2-chloro-4,5-dimethoxyphenyl)-butyrate with 30.0 gm. of redistilled ethyl oxalate in the presence of sodium ethylate (4.6 gm. of sodium and 11.70 cc. of absolute ethanol) under the usual conditions (1). The unchanged starting material (13.0 gm.) was separated by pouring the reaction mixture into ice and water and separating the ether layer. The glyoxylic ester was recovered by acidifying the aqueous solution of the sodio-salt with ice-cold 2 *N* sulphuric acid and extraction with ether. Removal of the solvent left 79.0 gm. of an oily ester which was decarboxylated by boiling with 18% sulphuric acid for 20 hr. The acid was dissolved in sodium bicarbonate solution and any suspended oil removed by extraction with ether. Acidification with 2 *N* sulphuric acid gave 41.9 gm. (74.5%) of the keto-acid melting at 76 to 77° C. Repeated crystallization of the acid from dilute acetic acid raised the melting point to 82° to 84° C. For analysis this was converted to the enol acetate (1).

A solution of 6.0 gm. of the keto-acid in 10 cc. of acetic acid and 10 cc. of acetic anhydride containing 0.4 gm. of fused zinc chloride was refluxed for two hours. The acetic anhydride was decomposed by the dropwise addition of water to the hot solution, and the enol acetate crystallized from the cold aqueous acetic acid solution. The enol acetate (70%) crystallized in rosettes of fine needles from benzene and melted at 141° to 142° C. Calc. for $C_{15}H_{17}O_6Cl$: C, 54.80; H, 5.21%. Found: C, 54.73, 54.74; H, 5.11, 5.22%. Saponification of the enol acetate regenerated the original keto-acid.

Cyclization of the keto-acid to 5-chloro-7,8-dimethoxy-3,4-dihydro-1-naphthoic acid was effected by vigorously stirring 34.6 gm. of the keto-acid with warm (80° C.) dilute sulphuric acid (145.0 cc. of concentrated sulphuric acid and 83.0 cc. of water) for 30 min. The cold reaction mixture was stirred into ice and water and the cyclized acid collected on a Büchner funnel, washed with water, and dissolved in a warm aqueous solution of sodium bicarbonate. Slow cooling of the solution yielded white platelets of the sodium salt which were collected and freed from resinous material by washing with acetone. Acidification of a warm aqueous solution of the sodium salt yielded 28.4 gm. (89.0%) of the solid acid melting at 154° to 156° C. Repeated crystallization of the acid from aqueous methanol gave the hemihydrate melting at 156° to 157° C. Calc. for $C_{13}H_{13}O_4Cl \cdot \frac{1}{2}H_2O$: C, 56.22; H, 4.72%. Found: C, 56.43, 56.23; H, 4.85, 4.80%.

The methyl ester was prepared in 98% yield by treating the acid with an ethereal solution of diazomethane. The resulting ester crystallized from aqueous methanol in fine needles and melted at 81° to 82° C. Calc. for $C_{14}H_{15}O_4Cl$: Cl, 12.54%. Found: Cl, 11.92%.

Methyl 1-Chloro-3,4-dimethoxy-7-ethoxyhexahydrophenanthrene-13-carboxylate

A solution of 24.0 gm. of 2-ethoxybutadiene-1,3 (3) and 0.4 gm. of hydroquinone in 60 cc. of sodium-dry toluene was heated in sealed tubes with 60.0 gm. of methyl 5-chloro-7,8-dimethoxy-3,4-dihydro-1-naphthoate at 195° to 210° C. for 90 hr. The contents of the tubes was fractionally distilled to remove the solvent and low boiling products as well as resinous materials. Recrystallization from aqueous methanol of the two main fractions, which boiled at 173° to 190° C. (3 mm.) and 190° to 230° C. (3 mm.) yielded 26.0 gm. of starting material and 10.0 gm. of the adduct as well as a residual 15.0 gm. which failed to crystallize in the time available for this work. The pure adduct crystallized in platelike crystals from aqueous methanol and melted at 162° to 165° C. Calc. for $C_{20}H_{25}O_5Cl$: C, 63.07; H, 6.61%. Found: C, 63.13, 63.22; H, 6.96, 6.77%.

Methyl 1-Chloro-3,4-dimethoxy-7-ketoöctahydrophenanthrene-13-carboxylate

The enol ethyl ether was hydrolyzed by dissolving 2.0 gm. of the adduct in 125 cc. of methanol and allowing this solution to stand at room temperature with dilute sulphuric acid (8.0 cc. of 6 *N* sulphuric acid and 12 cc. of water) for 1.5 hr. The reaction mixture was copiously diluted with water and the keto-ester extracted in ether, washed with water, and dried over anhydrous sodium sulphate. Removal of the solvent yielded a white solid residue which crystallized in long needles from aqueous methanol; yield, 1.5 gm. (81%); m.p. 159° to 160° C. Calc. for $C_{18}H_{21}O_5Cl$: C, 61.27; H, 6.00%. Found: C, 61.15, 61.05; H, 6.25, 6.24%.

The dinitrophenylhydrazone of the keto-ester crystallized from methanol in orange microcrystals and melted at 186.5° to 188.5° C. Calc. for $C_{24}H_{23}O_8N_4Cl$: N, 10.51%. Found: N, 10.53, 10.48%.

The oxime crystallized in fine silky needles from aqueous methanol and melted at 142° to 145° C. Calc. for $C_{18}H_{22}O_5NCl$: N, 3.81%. Found: N, 4.39%.

The diisonitroso derivative was prepared by dissolving 1.5 gm. of the keto-ester and 2.0 gm. of the amyl nitrite in acetic acid, previously saturated at 0° C. with dry hydrogen chloride gas (8). The reaction mixture soon turned yellow and after cooling to 0° C. for one hour it was allowed to stand at room temperature for six hours. The oil, which separated upon copious dilution of the reaction mixture with water, was extracted with three portions of ether and the extract washed with water and dried over anhydrous sodium sulphate. The solvent was removed on the steam bath (traces of amyl acetate were removed under vacuum), leaving 2.0 gm. of a brown resin which was soluble in 5% sodium hydroxide solution, methanol, and benzene, but insoluble in water and hexane. The resin was dissolved in benzene, clarified with Norit, and crystallized from this solvent by the addition of hexane. The resulting microcrystals gave a wine coloration with ferric chloride solution. The product proved difficult to purify and melted rather indefinitely at 175° to 180° C. Calc. for $C_{18}H_{19}O_7N_2Cl$: N, 6.81%. Found: N, 6.04%.

6,7-Dimethoxy-2-naphthoic acid

A solution of 28.6 gm. of ethyl γ -(2-chloro-4,5-dimethoxyphenyl)-butyrate in 70 cc. of sodium-dry ether was added dropwise to a suspension of sodium ethylate (2.3 gm. of sodium and 5.85 cc. of absolute ethanol) in 50 cc. of ether, cooled to -10°C . The ethyl formate (9.25 gm.) in 45 cc. of ether was added dropwise and the mixture allowed to warm up to 0°C ., when it was corked and left at 4°C . for five days. The deep red ethereal solution was poured into ice and water and the ether layer, containing unchanged starting material, was separated. The aqueous solution was acidified with 2 *N* sulphuric acid and the formylation product extracted with ether, washed with water and saturated brine solution, and then dried over anhydrous sodium sulphate. The crude formylation product, which gave a violet coloration with aqueous ferric chloride solution, was cyclized in sulphuric-phosphoric acid mixture (4). The recovered acid melted alone or on admixture with 6,7-dimethoxy-2-naphthoic acid at 242° to 244.5°C .

Cyclization of 12.9 gm. of the formylation product by a suspension of 28.5 gm. of phosphorus pentoxide in 80 cc. of boiling benzene (6) gave an acid which when crystallized from benzene melted alone or with 6,7-dimethoxy-2-naphthoic acid at 238° to 240°C . A Beilstein test for halogen was negative in both samples of the acid.

References

1. FIESER L. F. and HOLMES, H. L. J. Am. Chem. Soc. 60 : 2548. 1938.
2. GHOSH, R. and ROBINSON, R. J. Chem. Soc. 506. 1944.
3. HOLMES, H. L. and MANN, K. M. J. Am. Chem. Soc. 69 : 2000. 1947.
4. HOLMES, H. L. and TREVOY, L. W. Can. J. Research, B, 22 : 56. 1944.
5. HUDSON, B. J. F. and ROBINSON, R. J. Chem. Soc. 715. 1941.
6. PERKIN, W. H., JR., and ROBINSON, R. J. Chem. Soc. 105 : 2376. 1914.
7. SPEYER, E. and ROSENFELD, H. Ber. 58 : 1110. 1925.
8. WILLSTÄTTER, R. Ber., 30 : 2679. 1897.

THE PREPARATION OF BIS-NITROXYETHYLNITROÖXAMIDE^{1*}

BY R. S. STUART AND GEORGE F WRIGHT

Abstract

An economical method is described for preparation of the explosive *bis*-nitroxyethylnitroöxamide from oxalic acid and monoethanolamine. Yields over 80% of theoretical may be obtained from *bis*-hydroxyethyloxamide by either batch or continuous process. The crude product must be purified before use by acetone-water crystallization. The formation of this explosive is found to be inhibited by nitrosylsulphuric acid which limits the nitration to the *bis*-nitroxyethyloxamide stage. The complete reaction is thought to proceed via this intermediate by a nonreversible nitration and then to decompose reversibly, if allowed to proceed too long, to *bis*-hydroxyethylnitroöxamide. There is some evidence that the explosive is stabilized by its decomposition products. The use of this high explosive does not present the industrial health hazard caused by tetryl, with which it is comparable in power and brisance. Furthermore, it has the advantage over tetryl that it can be melted and poured. The solidified melt is unique among explosives because it is free from gross cavities.

A consideration of the thermochemistry of explosives shows that aromatic types such as trinitrotoluene, picric acid, and tetranitromethylaniline (tetryl) are necessarily less powerful than compounds which contain more hydrogen. The requirement of modern warfare indicated the need for new explosives possessing high power per unit weight and volume. Saturated aliphatic types of ready availability were therefore investigated.

Since a secondary explosive must carry the elements for its detonation to gaseous products (usually carbon monoxide and dioxide, nitrogen, and steam) within itself, it is evident that a compound with a carbon-hydrogen-oxygen ratio favorable to the production of these gases is desirable. The best known and most easily prepared explosives in the aliphatic series are the nitramines, the nitramides, and the nitrate esters. The present report describes the preparation and properties of *bis*-nitroxyethylnitroöxamide, which combines the latter two types.

This explosive was first described by Herz (4) as a very stable explosive, insensitive to shock. Neither of these claims is true. It is about 2.5 times as sensitive as trinitrotoluene. It decomposes at 105° C., but it melts at 91° to 92° C. and can be poured quite safely at this temperature. Furthermore it forms with T.N.T. a eutectic mixture melting at 61° C., and a composition of 79 parts of *bis*-nitroxyethylnitroöxamide with 19.5 parts of T.N.T. and 1.5 parts of beeswax forms a pourable slurry at 77° C. which solidifies to density 1.60 to 1.64 without formation of shrinkage cavities. This is largely owing to a tendency to supercool. This composition is only slightly more sensitive than pure T.N.T. Although its low melting point precludes its use as a service explosive, it is useful as an experimental mixture in explosives

¹ Manuscript received October 30, 1947.

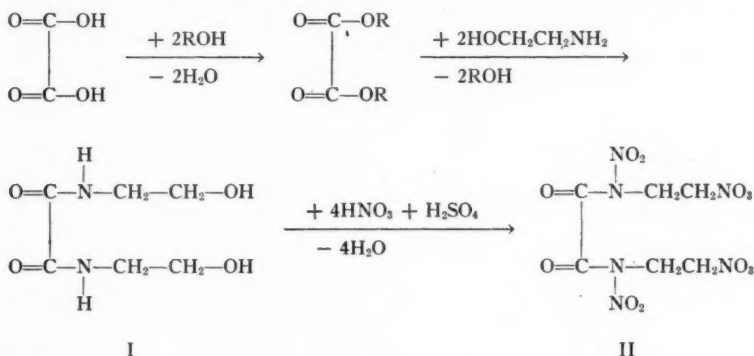
Contribution from the Chemical Laboratory, University of Toronto, Toronto, Ont. This research was requested and subsidized by the National Research Council of Canada.

* Reference has been made in the literature to the abbreviation NENO, used to designate *bis*-nitroxyethylnitroöxamide. Campbell, A. N. and Kushnarov, H. A., This Journal, 25 : 216. 1947.

EDITOR'S NOTE:—The subject of this paper has been released from security restrictions.

research. The power of this mixture is 1.25 times that of T.N.T. or about that of tetryl which is not a pourable explosive. The power of pure *bis*-nitroxyethylnitroöxamide is 1.31 times that of T.N.T.; its rate of detonation is 5400 m. per sec. at density of 1 and 7800 m. per sec. at density 1.60.

The preparation of *bis*-nitroxyethylnitroöxamide, II, involves the consumption of the available raw materials: oxalic acid, monoethanolamine, and nitric acids according to the following reaction scheme:



The intermediate amide, *bis*-hydroxyethyloxamide, I, can best be prepared from an ester of oxalic acid. The butyl rather than the methyl or ethyl ester was chosen, since no special entrainer would then be required in the esterification and recovery of the alcohol. It was found that crude sodium oxalate (93% pure), available commercially from the dehydrogenation of sodium formate, could be esterified in 90% yield by azeotropic distillation in butanol when slightly more sulphuric acid was used than was required to liberate the oxalic acid from its salt. No attempt was made to purify the dibutyloxalate except by simple distillation. Since butanol was used as the medium in the subsequent preparation of I, there was no need to remove this alcohol completely from the ester.

The purest and best yield of I was obtained by adding one equivalent of dibutyl oxalate to a well stirred solution of two equivalents of monoethanolamine in dry butanol. The temperature was kept below 37° C. A very efficient stirrer was needed because the product tended to cake on the walls of the vessel with consequent poor heat transfer. The reaction was completed, after addition, by heating the mixture to 98° C. for two hours. A 96% yield of fairly pure product was obtained by cooling and filtering the liquors. The impurities in this reaction liquor (ethanolamine oxalate and the half-ester) did not saturate it; hence the liquor could be re-used four or five times before the product was contaminated. A convenient operating method involved the removal, for total recovery by distillation, of part of this mother liquor. This was replaced by fresh butanol which had been used for washing of crude *bis*-hydroxyethyloxamide, I.

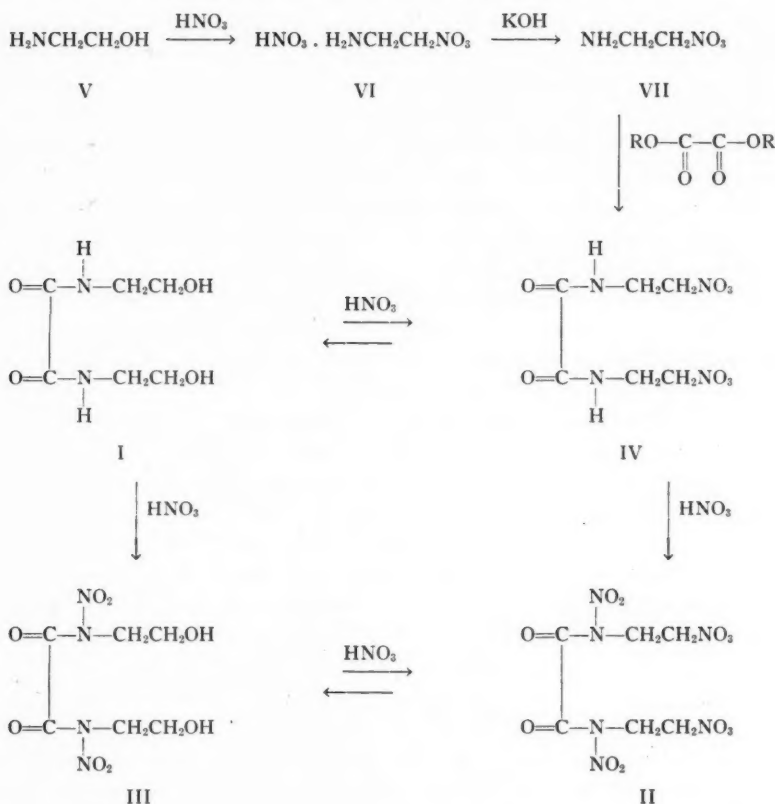
Proportionate addition of dibutyl oxalate and ethanolamine to butanol gave almost the same yield of good product. This more complicated procedure showed no advantage over the addition of dibutyl oxalate to ethanolamine described above. However a reverse order of addition, i.e., addition of ethanolamine to dibutyl oxalate in butanol gave a product that definitely was inferior.

Nitration of crude I (containing some occluded butanol and butyl oxalate) resulted in a low yield of II which was poor in quality. For this reason the crude I was dissolved in hot water and the butanol was distilled from this solution. The *bis*-hydroxyethyloxamide, I, which separated from the steamed liquor on cooling was a white solid, sufficiently pure for nitration. Since I is very soluble in water, about 5% of the original material remained in solution. This was not lost to the process since the relatively uncontaminated liquor could be re-used in subsequent steam distillations. In actual practice the liquor was used 20 times before it was necessary to discard it.

Trouble-free operation on the technical scale depends on an efficient stirrer, preferably one which scrapes the walls, thus ensuring good heat transfer. A large condensing surface is necessary for the steam distillation of butanol since the heat transfer through butanol-water films (especially on stainless steel) seems to be poor. Finally it is important to have proper decanting equipment to prevent loss of butanol owing to its solubility in water.

Previous work on the nitration of dimethyloxamide (1) has shown that maximum yields are obtained when the final concentration of sulphuric acid (with respect to total water) is that of sulphuric acid monohydrate. While *bis*-hydroxyethyloxamide, I, has also been nitrated successfully under these conditions, a better yield of purer product can be obtained by increasing the sulphuric acid concentration. A final concentration of 90% was found to be the most satisfactory (although *bis*-nitroxyethylnitroöxamide, II, was stable even in 93% aqueous sulphuric acid, for several days at room temperature). In order to achieve this final concentration of sulphuric acid, the initial acidity of the mixed acid had to be augmented by use of strong oleum and nitric acid. The use of this strong mixed acid was found not only to increase the yield but also the rate of nitration. These observations indicate that the over-all process for preparation of II resembles the nitrate esterification of compounds like penta-erythritol and glycerol more than the nitration of simple unsubstituted alkylamides.

There are two possible paths by which *bis*-hydroxyethyloxamide, I, can be converted to II. These paths have been outlined in the formulation, page 404. If nitroxylation of the hydroxyl groups of I were first to occur, then *bis*-nitroxyethyloxamide, IV, would be formed as an intermediate. Nitration of IV would then lead to II. Alternatively, the order of these steps might be reversed so that *bis*-hydroxyethylnitroöxamide, III, was the intermediate.



The synthesis of one of these two possible intermediates has been effected by nitroxylation of monoethanolamine, V. The nitroxyethylammonium nitrate, VI, which is thus formed can be converted to the free base, VII, by cautious treatment with alkali. This base, when added to diamyl oxalate, forms IV. The same compound is formed in good yield when I is treated with four moles of absolute nitric acid at 0° C.

This compound IV is unstable in aqueous sulphuric acid stronger than 85%. Although sulphuric acid of higher concentration increases this instability, the addition of either nitric or nitrosylsulphuric acid has a marked stabilizing effect. The presence of nitric acid in the sulphuric acid leads to formation of *bis*-nitroxyethylnitroöxamide, II, in 75% yield, but nitrosylsulphuric acid inhibits this reaction, and IV can be recovered in good yield. As might then be expected, when *bis*-hydroxyethyloxamide, I, was treated with mixed acid containing 1% of nitrosylsulphuric, a 77% yield of IV was obtained without contamination by II. This would indicate that nitrous acid inhibited the nitration of IV to II.

This does not demonstrate that, in absence of nitrous acid, IV is an intermediate in the formation of II from I. Indeed, there is evidence that III is involved in the reaction, although this compound has never been isolated as a chemical individual. This may be owing to its reactivity and also to its solubility, which might be expected to be high in water.

The evidence that *bis*-hydroxyethylnitroöxamide, III, is involved in the reaction is indirect. The yield of II from I is never higher than 87% of theoretical. This number also designates the extent of recovery if II is dissolved in a mixed acid of the same composition as that which obtains at the end of a normal nitration. This suggests that the yield of II depends on an equilibrium reaction. Esterification such as that of $I \rightleftharpoons IV$ or $III \rightleftharpoons II$ is known to be a type of reaction that reaches a measurable equilibrium. So far as is known, on the other hand, amine nitration is irreversible with respect to an N-alkyl acid amide and a nitric-sulphuric acid mixture.

There is further evidence for the equilibrium state at the end of reaction $I \rightarrow II$. If nitration was carried out in a mixed acid initially containing 18 moles of nitric acid per mole of *bis*-hydroxyethyloxamide, I, a second phase separated after half the reaction time had elapsed. If, at the end of the reaction period, the two phases were processed separately, the upper phase was found to be relatively pure II and nitric acid. The phase containing sulphuric acid, on the other hand, yielded a much less pure II when it was diluted with iced water. When this impure II was added to fresh mixed acid, its purity was markedly enhanced.* This indicates that an equilibrium state exists in the spent mixed acid, and that a mixture of II with III is precipitated by addition of water.

While it thus seems probable that an equilibrium state exists in the formation of *bis*-nitroxyethylnitroöxamide, II, it does not necessarily follow that III is the intermediate in the nitration process. Indeed there is evidence that the reaction follows the irreversible path $I \rightarrow IV \rightarrow II$ and that subsequently the reversible reaction $II \rightleftharpoons III$ is involved. The formation of II is slow enough that the yield and purity can be evaluated with respect to time. The data, plotted with respect to melting point in Fig. 1 and to yield in Fig. 2 show that the optimum in each is attained in about 45 min. after which both yield and quality fall off. These types of curve are typical for all concentrations and ratios of mixed acid which were used. The impure product which is obtained after two hours' reaction time can be brought to the purity of the product obtained after 45 min. simply by dissolving it in fresh nitrating acid and reprecipitating into iced water after the optimum reaction period.

Evidently the contaminant cannot be I because it is much more soluble in aqueous media than in II. Since this contaminant seems to be reversibly convertible to II it must be III rather than IV, because the reaction $IV \rightarrow II$ is an amine nitration supposedly irreversible. However, the shape of the

* Advantage was taken of the phase separation in our continuous nitration process, and the impure II from the diluted acid phase was returned to the beginning of the cycle.

curves in Figs. 1 and 2 indicate that several reactions are proceeding, of which only the slowest reaction is reversible. It follows, then, that the initial nitration path is $I \rightleftharpoons IV \rightarrow II$ which is followed by the undesirable side reaction $II \rightarrow III$. The rate-controlling step is probably $I \rightleftharpoons IV$, since amine nitration is thought to be a fast reaction compared with esterification.

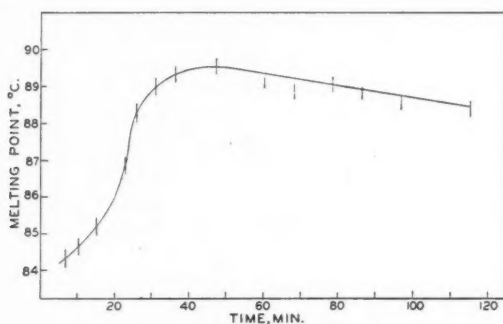


FIG. 1. Effect on melting point.

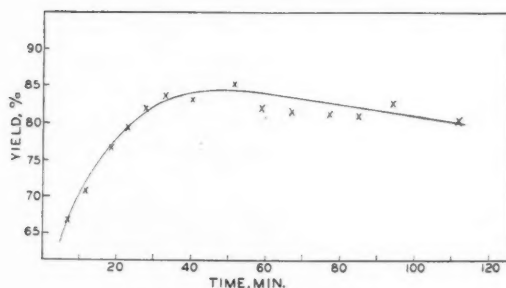


FIG. 2. Effect on yield.

The nitration of I to II can be carried out as a batch or a continuous process. The continuous process would seem to have an advantage over the batch method in that the heat of dilution of reaction liquor into water can be dispersed gradually during the reaction period rather than at once at the end of the batch process. This apparent advantage no longer applies if the batch product is diluted into 93% sulphuric acid, in which II is both stable and insoluble. Indeed an economy is effected by such dilution, since the sulphuric acid serves also for partial fortification of the spent acid prior to recovery. The impurities in this fortified spent acid decompose so readily that recovery of nitric and sulphuric acid does not present an abnormal technical problem.

The continuous process does, however, lend itself more easily to economical operation with low ratios of nitric acid to *bis*-hydroxyethyloxamide, I. As the ratio $HNO_3 : I$ is decreased from 20 : 1 to 12 : 1, the melting point of the entire product is decreased from 89° to 83° C. In the continuous process it

is, however, simple to effect a separation of this product into a high melting (m.p. 89° C.) phase and a phase which, on dilution, yields impure material melting below 80° C. This impure I can be purified by solution in the nitric acid which is fed initially into the continuous nitrator. The extent of this phase separation is outlined in Table I.

TABLE I
PHASE SEPARATION IN NITRATION OF
bis-HYDROXYETHYLOXAMIDE (I)

Ratio HNO ₃ /I	Organic phase, % yield	Acid phase, % yield
12 : 1	75	7
13.8 : 1	64	21
15 : 1	46	47
20 : 1	0	87

It may thus be seen that the continuous process may be slightly advantageous with low ratios of nitric acid to I but that either is equally good when a 20 : 1 ratio is employed.

Since the yields are essentially the same over a wide range of operating conditions the choice of a nitrating acid depends on the materials which are economically available. The final concentration of sulphuric acid should not drop below 90% and this requires an initial acid which is essentially anhydrous. Actually optimum rate is attained when the mixed acid has an apparent total acidity of $101 \pm 0.5\%$. The acid mixtures which will meet this requirement for the several ratios of nitric acid to *bis*-hydroxyethyloxamide are shown in Table II, together with the yields and reaction times which correspond. It should be noted that these mixed acids require nitric acid which is at least 95% pure until such time as oleum containing more than 40% SO₃ becomes commercially available.

TABLE II
NITRATING ACIDS USING 40% OLEUM

Molar ratio $\frac{\text{HNO}_3}{\text{I}}$	Final weight ratio $\frac{\text{H}_2\text{SO}_4^*}{\text{H}_2\text{SO}_4 + \text{H}_2\text{O}}$	Initial HNO ₃ conc. %	Mixed acid		Reaction time, min.	% yield NENO
			HNO ₃ %	H ₂ SO ₄ %		
10 : 1	1.00	—	62.6	37.7	120	77
12 : 1	1.09	94.5	56.0	45.0	65	82
13.8 : 1	1.08	96.4	61.5	39.5	55	84
15 : 1	1.08	97.2	65.3	35.7	50	83
20 : 1 A	1.00	98.0	77.8	22.5	45	87
20 : 1 B	1.16	94.8	52.8	48.2	25	86

* Ratio is that of anhydrous sulphuric acid to its monohydrate.

Experimental*

Dibutyl Oxalate

Into a 3-liter three-necked flask (equipped with Hershberg stirrer, mercury seal, and reflux through a decanter) containing 1 liter (9.3 moles) of technical butanol is added 125 cc. (2.17 moles) of 93% sulphuric acid and then 400 gm. (1.87 moles) of wet crude sodium oxalate containing 67.5% of solids†. The stirring is continued while the slurry is heated to boiling (oil bath) and water is continuously removed through the decanter, which returns the butanol to the flask. This removal of water is complete in 15 hr. at our rate of heating; 220 gm. of water is recovered. The reaction mixture is cooled to 80° C. and treated quickly with the minimum (470 cc.) of aqueous distillate necessary to dissolve the suspended sodium sulphate. After separation of the aqueous layer, the nonaqueous layer is washed with a small amount of cold water. It is then distilled to yield 590 cc. of recoverable butanol (b.p. 105° to 145° C., d_4^{20} 0.83) and finally to yield 350 cc. (d_4^{20} 0.98) of dibutyl oxalate, b.p. 238° to 244° C., sapn. equiv., 101 (calc. 102). This represents a yield which is 90% of theoretical.

Bis-hydroxyethyloxamide

A solution of 122 gm. (2 moles) of monoethanolamine in 3345 gm. (4.52 moles) of fresh or recovered butanol is stirred and cooled so that the temperature remains below 37° C. while 202 gm. (1 mole) of dibutyl oxalate is added over 20 min. The resulting slurry should be heated to 98° C. over two hours, then cooled with vigorous stirring and filtered by suction. A 95 to 98% yield (wt. 169 to 174 gm., m.p. 168° to 169° C. when washed with ethanol) is thus produced; the butanol filtrate contains 2 to 5% of impure product, m.p. 136° to 144° C. as a 0.8 to 0.9% solution. This small amount is not isolated, instead one-fifth of the butanol solution is replaced by fresh (washing) butanol, and the filtrate then is used as the solvent medium for a subsequent preparation. The one-fifth which is removed is totally evaporated and the residue discarded.

Although this procedure gives a good yield of pure product, a very efficient stirrer is required to manipulate the mixture before it is heated. If such a stirrer is not available, proportionate addition of the ethanolamine and dibutyl oxalate gives a product which is nearly as good as that obtained by the one-feed addition; the mixture is much easier to stir.

In order to free the crude product from butanol, the crude material is suspended in its own weight of water and steam distilled to remove the alcohol. The residual solution is cooled with stirring to give 97% of the original material, m.p. 168° to 169.5° C. If the aqueous liquor is evaporated to dryness it yields the remainder melting at 160° to 164° C. However, the concentration of impurity is so low that in practice this liquor is used

* All melting points have been corrected against reliable standards.

† This material was kindly supplied by Imperial Chemical Industries from their plant in Widnes, Lancashire.

repeatedly for subsequent crystallization until the principal product shows contamination after about 20 cycles. The chief impurity is ethanolamine oxalate; m.p. 195° to 200° C.

The purified *bis*-hydroxyethyloxamide should be dried (air draft at 40° C.) until it contains less than 0.1% moisture, and should be stored in a dry place.

Bis-nitroxyethyloxamide, IV

A solution of 16.9 gm. (0.1 mole) of nitroxyethylammonium nitrate (2) in 100 cc. absolute ethanol containing 5.6 gm. (0.1 mole) of potassium hydroxide is treated with 11.3 gm. (0.05 mole) of diamyloxalate. Cautious dilution with water yields 13.3 gm. of nitroxyethyloxamide, m.p. 144° C. This 50% yield is purified by solution in 90% nitric and cautious precipitation into ice. It then melts at 148.2° C. Calc. for $C_6H_{10}N_4O_8$: C, 27.1; H, 3.79%. Found: C, 27.1; H, 3.81%.

The same compound is obtained in 98% yield when 0.026 mole of *bis*-hydroxyethyloxamide, I, is treated with 0.366 mole of absolute nitric acid for three hours at 0° C. Addition of 0.25 mole of phosphoric acid (85%) does not change this yield, but the same amount (0.25 mole) of 95% sulphuric converts the nitric acid solution of IV in 75% yield to *bis*-nitroxyethylnitrooxamide, m.p. 85.5° C. When 0.26 mole of I is added slowly to a stirred mixed acid at 25° C. containing 5 moles of absolute nitric acid and 1.04 moles of absolute sulphuric acid with 0.1 mole of nitrogen tetroxide, a 77% yield of IV is obtained. If the nitrogen tetroxide were absent, an 85% yield of II would have resulted.

Bis-nitroxyethylnitrooxamide

A. Continuous Process

The type of continuous nitrator which we used is illustrated in Fig. 3. Unit A is a U-shaped tubular mixing chamber equipped with screw feeder, G, (which contains and feeds the *bis*-hydroxyethyloxamide, I), mixed acid feeder, V, and stirrer, I. This requires two motor drives for the solids feeder and one for the stirrer. The mixing chamber is cooled by water sprays, U and K, and by water jacket; it could have been constructed from iron rather than stainless steel. A feeder, T, was introduced into its exit leg in order to introduce a nitric acid solution of impure II from a former run, when such purification was necessary. The feed rate for the solid, I, was adjusted by the speed of the motor which rotated the screw-feeding Irwin bit. The liquid feeds were controlled through a stainless steel proportioning pump.

The reaction mixture emptied from this mixing chamber into Units B, C, D, and E. These were constructed from 1 in. iron pipe equipped with loose-fitting glass plates and thermometers and heated externally to 40° C. by water sprays. These units served to hold the mixture until the time when reaction had proceeded to the point of phase separation. They emptied into Unit F (a kettle which could have been made from iron rather than stainless steel) which served for phase separation, or simply for additional holding time

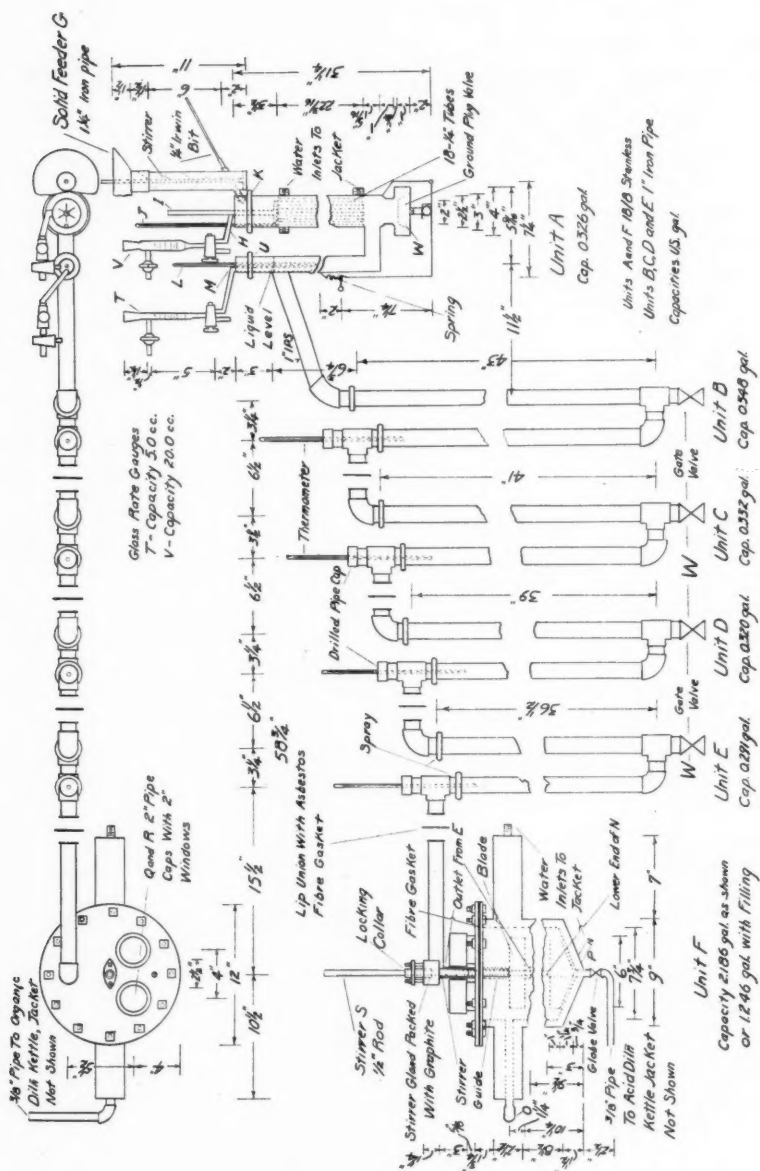


FIG. 3. Continuous nitrator.

until the reaction mixture was valved into a stirred water-dilution vessel. The original volume (2.186 U.S. gal.) of Unit *F* could be reduced to 1.246 gal. by insertion of packing material.

The quantity of mixed acid, as well as the reaction time, determined the necessary volume of the system. Sometimes, as in the case of the 13.8 : 1 ratio of nitric acid to *bis*-hydroxyethyloxamide presently to be described, Unit *B* fed directly into Unit *F* to reduce the total reactor volume to 1.92 gal., not including *F*.

A separatory-recycling procedure employing the ratio HNO_3/I of 13.8/1 will be described as a 24 hr. operation. On the basis that the machine already was filled with reaction mixture, 23.0 lb. (60 moles) of *bis*-hydroxyethyloxamide, I, was introduced in 0.194 lb. (0.5 mole) batches via the screw-conveyor feeder, *G*, every 12 min. During the 24 hr. period 175.5 lb. of mixed acid (58.2% HNO_3 , 43% H_2SO_4) at 20° C. was added through sight-feeder *V* by a stainless-steel Hills-McCanna metering pump, type RM-2FD. This pump also metered 18 lb. (containing 6.05 lb. of II) of 98% nitric acid solution through sight-feeder *T*. The temperature of the inlet was maintained below 35° C. while the remainder of the equipment was warmed to 38°–40° C. to maintain reaction rate and to prevent solidification of II in the reaction system.

The liquid was allowed to settle without stirring in Unit *F*. Adjustment of the bottom valve, *P*, allowed withdrawal of the mixed acid layer into water or sulphuric acid (either of which would precipitate the impure II) at such a rate that the upper, organic layer drained into drowning water from the outlet *O*, and still maintained a layer about 1 in. thick. Both dilution kettles were cooled to 15° C. When the acid layer was diluted into 93% sulphuric acid, 111.6 lb. was used every eight hours. Over the same period 26 lb. of water was used to solidify the organic layer.

Both suspensions could be filtered and washed with water (to bromcresol green neutrality) to give a 39.8 lb. (84.8% of theory) yield of *bis*-nitroxyethylnitrooxamide, II, melting at 88° to 89° C. It should be noted, however, that 5.52 lb. of this was obtained from the mixed acid layer. Any impure II resulting from unsatisfactory raw materials or process control will concentrate in this portion. Its weight is slightly less than the amount of impure II used in the recycling procedure just described. The process is therefore self-regulating in continuity. The recycling solution may be prepared by dissolving impure II in 2.9 parts of 97 to 98% nitric acid. This solution takes place with so much absorption of heat that it is necessary to warm the nitric acid. The process does not, of course, depend on the recycling feature and nitric acid alone may be added at *M*.

The entire system illustrated in Fig. 3 was used for the 20 : 1 (*B*) HNO_3/bis -hydroxyethyloxamide ratio (see Table II), but Unit *E* was eliminated from the equipment when the 20 : 1 (*A*) mixture was used. No phase separa-

tion occurred with either of these mixtures, and Unit *F* acted only as a conduit to lead them directly to dilution, usually in 93% sulphuric acid. The yields of II were slightly higher than the 84.8% recorded for the 13.8 : 1 ratio.

The heat of dilution of the reaction mixture into 93% sulphuric acid is so much less than that of the reaction mixture into water that a batch process can be equally satisfactory with the continuous one. The batch reaction is carried out according to the reaction times shown in Table II; these times are regulated by the length of the reactor system in the case of the continuous process.

B. Batch Process

The experimental batch processes were carried out in Unit *F* alone when it was equipped with stirrer, thermometer well and two 2-in. ports through which *bis*-hydroxyethylxamide, I, could be added and observation made. The 13.8/1 HNO_3 : I ratio was used in this manner by adding 1.9 lb. (4.84 moles) of I (m.p. 165° to 168° C.) with stirring and jacket cooling, at 40° C. to 15.2 lb. of mixed acid (61.6% HNO_3 , 39.7% H_2SO_4) over a 45 min. period. After subsequent stirring at 40° C. for 15 min. the mixture was cooled to 20° C. with stirring and then was valved into 8.56 lb. of 93% sulphuric acid, which was stirred and cooled to maintain a dilution temperature of 25° to 30° C.

The slurry could be filtered by suction through glass or stainless steel cloth, but a stainless steel centrifuge was much more convenient, and safe if the product, II, was not dried below 20% wetness. The washing procedure was the same with either filtering device: successive washes of 85, 70, 50, and 25% aqueous sulphuric acid were used and advanced to the next higher strength category after passage through the product, II. The final washing was with water, ultimately to a residual acidity not greater than bromocresol green neutrality.

The use of sulphuric acid as a diluent was convenient since it also conditioned the waste acid for recovery of the nitric acid excess. Distillation of these butted waste acids proceeded quietly with a gradual temperature rise to 85° to 100° C., when 93 to 97% nitric acid distilled over. Final heating to 180° to 200° C. expelled a small amount of nitrogen oxides.

C. Purification of II

The purification of *bis*-nitroxyethylnitroxamide, II, can be carried out in the laboratory by solution in *cis*-dichloroethylene (b.p. 55° to 60° C.) over 10 min. boiling. One gram is soluble in 5 cc. to which 0.01 gm. of calcium carbonate is added. After chilling, the crystal crop is filtered off to weigh 0.85 to 0.90 gm. This pure II melts at 91° to 92° C. Its Abel Heat Test at 100° C. is 25 to 30 min. Calc. for $\text{C}_6\text{H}_8\text{N}_6\text{O}_{12}$: C, 20.2; H, 2.26%. Found: C, 20.2; H, 2.28%.

This purification is obviously not adapted to the large scale, and a hot-water treatment followed by precipitation of acetone by water is used instead. The crude II, containing 30 to 35% moisture, need not be dry for this purification. Its water content must, however, be known. A 1 to 3 gm. aliquot

is melted in a tared 150 mm. test tube and then solidified as a layer on its wall. Most of the water phase is decanted off; the remainder is removed by evacuating the tube while it is cautiously immersed in the steam bath. Spattering is thus avoided, and dehydration is complete after four minutes.

On the basis of the dry weight so obtained the crude, wet II is melted by addition to water maintained at 100° C. by a wet-steam jacket. Temperatures higher than 100° C. must be avoided. When the crude product is spread over the surface of the water, there is no tendency toward lumpiness of the solid, and fusion is therefore rapid. One kilogram of material spread over the circular surface of a steam-jacketted melter containing 2 liters of water is melted over the three minutes required to add it. When fusion is complete, the steam heating is discontinued, and the heavy cloudy layer of molten II is drawn off into 96 to 100% acetone (1700 cc. per kilo dry weight of II). To the warm acetone solution is added 50 gm. of precipitated calcium carbonate per kilo of II. After stirring for 15 to 60 min. (test portion in water should be neutral to bromcresol green) the solution is filtered through a Celite bed.

Bis-nitroxyethylnitroöxamide, II, evidently exists in two polymorphic forms, of which the α (needle habit) is stable at room temperature while the β (massive habit) is stable at higher temperatures. The β -form is desirable if high density of packing (0.85 to 0.95) must be attained; it also seems to be less sensitive to impact than the α -form. A crystallized product containing largely the β -form can be obtained by observing the following crystallization schedule.

The acetone solution is stirred *rapidly* while $1\frac{1}{2}$ times its volume of water is added over one hour. The initial temperatures of acetone solution and water should be 28° C. The first fifth of the water may be added rapidly (five minutes). The second fifth should be added over 20 min., during which time the temperature will reach 32° C. and crystallization will begin. The temperature will increase further to about 34° C. A separate oily phase appears, in which crystal growth will occur. It is well to seed with the β -form when this second phase appears, in order that crystal growth will occur smoothly within it so as to avoid supersaturation. The last three-fifths of the diluent water may be added over the remaining 35 min. It may be somewhat cooler in order that the temperature will not exceed 34° C. Lumping and wall-caking will occur if the temperature exceeds 34° C.

This ought to produce a granular product which will dry easily under forced-air draft at 40° C., and will pack to a bulk density of 0.85 to 0.95. If inattention to temperature or addition rate tends to produce a finer product containing much α -polymorph (as seen in a microscopic, needle versus massive, crystal count) the batch can be improved, prior to filtration, by digesting it at 38° C. for one hour. This causes a 4% hydrolytic loss.

The dry product contains less than 0.1% moisture and melts at 90° to 91° C. The melt or acetone solution may be turbid, but the calcium oxalate which causes this turbidity may be avoided by use of distilled water for the

crystallization. The product shows an Abel Heat Test at 100° C. of 10 to 15 minutes. Titration with alkali using brom-thymol blue as indicator shows less than 0.01% acidity; only the first color change is significant, since II tends to hydrolyze in presence of alkali. Finally the compound evolves not more than 4 cc. of gas during a six-hour vacuum stability test (3) at 100° C.

Explosive of this quality is nonhygroscopic and can be melted and poured without gassing after at least four years of ordinary storage. The most useful mixture for munitions filling has been a 79 : 19.5 : 1.5 mixture of II with T.N.T. and beeswax. This is prepared by melting the T.N.T. and beeswax at 80° to 85° C., then stirring in the granular II to give a final slurry not hotter than 78° C. This slurry cools almost to room temperature before solidification is complete. It is therefore dense (1.60 to 1.64) and entirely free from cavities. For these reasons it is useful in experimental fillings, but its softening point (61° C.) is somewhat low for service use.

No health hazards have been encountered after four years' use of *bis*-nitroxyethylnitroöxamide. It does not stain the hands nor cause dermatitis as does tetryl. Since it is slightly more sensitive and more powerful than this commonly used explosive, and it stems into pellets or channels as well as does tetryl, it may be used to replace it as a primary or initiating explosive.

References

1. ALLENBY, O. C. W. and WRIGHT, G. F. Can. J. Research, B, 25 : 295. 1947.
2. AUBRY. Mém. poudres, 25 : 194. 1932-33.
3. FARMER, R. C. J. Chem. Soc. 117 : 1432. 1920.
4. HERZ, E. v. German Patent 543,174. Nov. 6, 1930. Abstracted in Chem. Abstracts, 26 : 2598. 1932.

THE THERMAL DECOMPOSITION OF CARBOHYDRATES¹

I. E. PUDDINGTON

Abstract

The thermal decompositions of cellobiose, maltose, dextrose, and potato starch have been studied over a temperature range, by following the production of volatile products. Carbon dioxide, carbon monoxide, and water with small quantities of acids, aldehydes, and volatile solids were produced in all cases. With cellobiose, the first step of the reaction, which involved the elimination of two moles of water per mole of sugar, could be separated from the second step, where the oxides of carbon were produced, by controlling the reaction temperature. Dextrose first dimerized by a rapid reaction and then decomposed in much the same manner as cellobiose. The behavior of maltose was anomalous and no dehydration by a separate step could be detected. The decomposition of potato starch was similar to the second step of the cellobiose reaction.

Introduction

While following the dextrinization of potato starch in the absence of catalysts, it was observed that the reaction proceeded much more rapidly if the starch were maintained at reduced pressure instead of being exposed to the atmosphere in an open container. It was also noted that water and a permanent gas were produced during the reaction. This suggested that the process of dextrinization is a thermal decomposition, and that the accelerated rate that was noted at the reduced pressure was due to the removal of the gaseous products from the surface of the reacting solid. A review of the literature indicated that while changes in the character of the solid product have been carefully followed when starch is heated, little attention has been paid to the gases evolved, and the above observations appeared to be sufficiently novel to warrant a more detailed study. The behavior of some of the simpler carbohydrate molecules has also been investigated, and the present paper describes the results obtained with dextrose, cellobiose, and maltose as well as those from starch.

Experimental Procedure

Analysis of the gaseous products formed during the decomposition of several carbohydrates showed them to be composed of carbon dioxide and carbon monoxide, and the apparatus shown in Fig. 1 was devised and constructed to follow the rate of reaction and the composition of the products. The apparatus consisted of a reaction bulb connected, through suitable collecting traps and pressure measuring devices, to a continuous diffusion collecting pump capable of maintaining a pressure of 10^{-5} mm. of mercury continuously (12). The reaction bulb was contained in a furnace, the temperature of which was automatically controlled to $\pm 0.5^\circ$ C.

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In making a run, a weighed sample of carbohydrate was placed in the reaction bulb and the pressure in the system reduced to 10^{-4} mm. with external vacuum pumps. The trap adjacent to the reaction bulb was then surrounded with liquid air, the furnace placed over the reaction bulb and the diffusion collecting pump started. Water and carbon dioxide produced by the reaction were trapped by the liquid air, while the carbon monoxide passed on to the gas reservoir of the collecting pump.

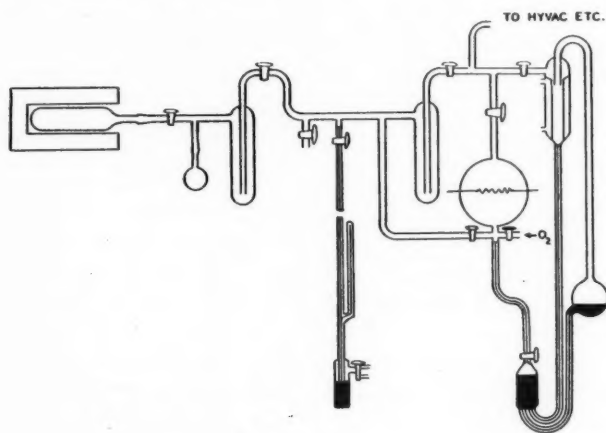


FIG. 1. *Apparatus.*

From time to time the run was interrupted and the reaction products were analyzed. While this was being done the stopcock adjacent to the reaction vessel was closed and a trap between it and the reaction bulb (not shown in the diagram) was surrounded with liquid air to maintain a low pressure in the reaction bulb. Carbon dioxide and water were separated by distillation, the water being collected in the removable bulb and weighed, while the carbon dioxide was collected in the second trap. If the run had been a particularly long one, the gas in the reservoir was recycled through the second trap to ensure a complete separation of the carbon dioxide from the carbon monoxide. The volume of carbon dioxide was then determined by measuring the pressure in the second trap when the gas was expanded to room temperature. The carbon monoxide was determined by expanding it into the combustion chamber and burning it on a platinum filament, after the admission of excess oxygen; the carbon dioxide thus formed could then be collected and determined in the second trap. When an analysis was completed the system was again evacuated and the run continued. This procedure gave a reasonably precise method for determining the amounts of the reaction products. Results from run to run agreed to within 5%, which was considered satisfactory for a reaction of this sort.

The rate of formation of products per gram of carbohydrate was independent of the size of sample, and the reactions were substantially first order. Activation energies, where given, were calculated from the slopes of the straight lines obtained when the logarithms of the times required to reach various percentages of product were plotted against the reciprocal of the absolute temperature of the reaction.

Cellobiose

The cellobiose used was obtained from the Difco Laboratories, Inc.

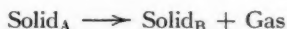
The variation in the rate of reaction and in the products over the temperature range of 210° to 240° C. is shown in Table I. That the reaction is mainly a dehydration is shown by the large amount of water produced, compared to the carbon dioxide and carbon monoxide; this eventually reaches a

TABLE I
VARIATION IN THE DECOMPOSITION WITH TEMPERATURE

Temp., °C.	Time, hr.	Volatile products produced		
		H ₂ O, %	CO ₂ , cc./gm. at N.T.P.	CO, cc./gm. at N.T.P.
210	1	1.23	0.069	0.014
	5	3.33	0.386	0.083
	7.5	4.98	0.731	0.152
	10.5	6.81	1.103	0.221
	13.5	8.44	1.496	0.290
	16.5	9.83	1.933	0.380
	19.5	10.91	2.292	0.463
	22.5	12.03	2.637	0.546
	26.5	12.93	3.030	0.649
	30.5	13.68	3.423	0.794
	34.5	14.48	3.829	0.897
	36.5	14.89	4.063	0.966
220	2	4.80	0.510	0.132
	4	8.71	1.064	0.240
	6	10.50	1.640	0.345
	8	11.55	2.200	0.468
	10	12.40	2.721	0.580
	12	13.15	3.200	0.700
	14	13.81	3.595	0.817
	16	14.50	3.980	0.935
230	0.33	2.69	0.205	0.036
	1.08	8.65	0.868	0.127
	1.66	10.96	1.350	0.204
	2.67	11.92	1.887	0.343
	4.00	12.83	2.654	0.469
	5.50	13.85	3.395	0.662
	7.25	15.19	4.261	0.818
240	0.25	7.53	0.380	0.124
	0.58	10.77	1.130	0.274
	1.00	11.86	1.880	0.417
	1.66	13.07	2.692	0.591
	3.08	14.95	4.107	0.946
	48	27.1	15.3	4.2

molecular ratio of approximately 64 : 4 : 1. It has been found convenient to express the amount of water as a percentage of the original cellobiose while the gaseous products are given in cubic centimeters per gram at N.T.P.

Fig. 2 shows graphically the rate of production of carbon dioxide at the different temperatures. The sigmoid type of curve which is usually found for reactions of the type



when pressure vs. time plots are made (2) is shown only at the lower temperatures, and even here only a slight induction period can be observed. This may be due to the finely divided state of the solid, while its complete disappearance at the higher temperatures is probably due to the fact that the melting point of cellobiose has been exceeded.

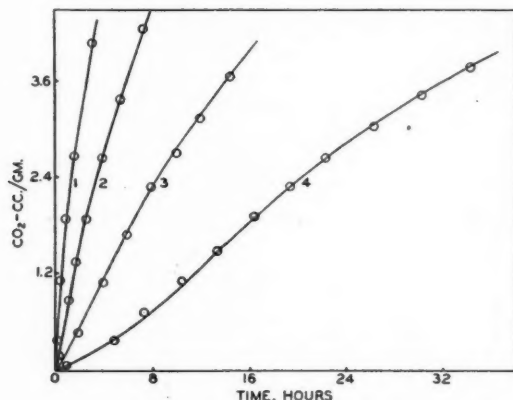
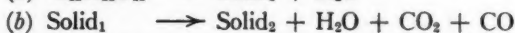


FIG. 2. Effect of temperature on the rate of production of carbon dioxide. Curves 1, 2, 3, and 4 represent respectively the results obtained with cellobiose at 240°, 230°, 220°, and 210° C.

The variation in the ratio of the products as the reaction temperature is changed is shown in Fig. 3. It is apparent from this figure that two reactions that have widely different temperature coefficients are taking place. The first of these reactions is a dehydration, and extrapolation indicates that the amount of water lost is approximately two moles of water per mole of sugar. The second reaction involves the production of water, carbon dioxide, and carbon monoxide from the solid product of the first reaction. The constant ratio of $\text{CO}_2/\text{H}_2\text{O}$ for the second reaction was maintained as long as decomposition could be conveniently followed. The process may be represented as follows:



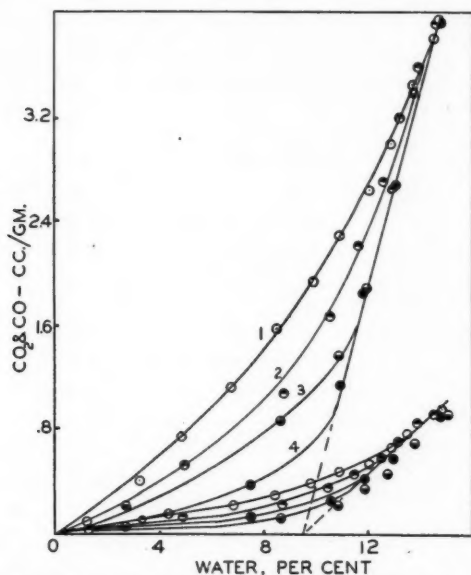


FIG. 3. Variation in product ratio with temperature. Curves 1, 2, 3, and 4 represent respectively the production of carbon dioxide from cellobiose at 210°, 220°, 230°, and 240° C.; unnumbered curves represent production of carbon monoxide in the same temperature order.

The decrease in water solubility of the solid product of these reactions and the horny appearance of the product suggest that polymerization has taken place. The similarity of the decomposition of this material to the behavior of starch under similar treatment is also indicative of this.

Confirmation of the existence of two reactions having different temperature coefficients is illustrated in Fig. 4, which shows a sudden decrease in the over-

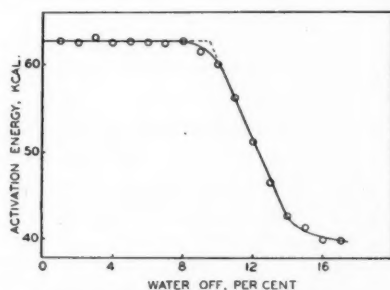


FIG. 4. Variation in activation energy of the cellobiose decomposition with degree of reaction.

all activation energy of the reaction after slightly less than 10% of water has been lost by the cellobiose. There is an indication that the activation energy is approaching a constant value again in the vicinity of 40 kcal. Fig. 5

indicates that carrying the reaction out at a temperature in excess of 255° C. would completely separate the two reactions and allow Step (a) to go to completion before any substantial amount of carbon dioxide is lost from the mixture.

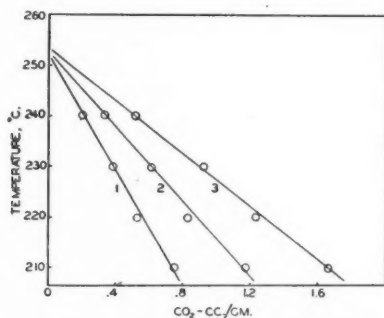


FIG. 5. The effect of temperature on the carbon dioxide produced from cellobiose at constant degree of dehydration. Curves 1, 2, and 3 represent values at 5, 7, and 9% of water given off.

During the reaction a small amount of a white crystalline product and an amber colored syrup distilled from the reaction vessel and collected in the tubing just outside the furnace. These products would partially account for the difference between the 1.9 moles of water found from Step (a) of the reaction and the 2 moles which would seem more likely. No accurate determination of this distillate was made owing to the difficulty of removing the deposit quantitatively. The water collected usually contained small quantities (about 1 to 2%) of a substance that gave qualitative tests for formic acid, and a polymerizable material, possibly furfural. These are included in the water percentage. It is also possible that the carbon monoxide fraction contained small quantities of methane.

While postulating a mechanism for the thermal decomposition of solid potassium and silver permanganates Prout and Tompkins (10, 11) point out that since solid decompositions are surface reactions, the excessive strains set up if Solid 2 has a different crystal form from Solid 1 should produce fissures, and a greatly accelerated decomposition rate following an induction period should occur. Mutual interference of the fissures should eventually cause a decay in the reaction rate. This would explain the sigmoid curve which was found experimentally in a pressure-time plot of their data.

The equation derived from their work

$$\log \frac{p}{p_f - p} = k \log t + c,$$

where p_f is the final pressure and t the time, was obeyed over their whole pressure-time curve, with an abrupt change in the k value at the inflection point, which represents the change-over from the acceleration to the decay period. Since this same equation fits the data in Curve 4 of Fig. 2 which

represents about 25% of the cellobiose decomposition, Prout and Tompkins' mechanism would appear to be applicable to the thermal decomposition of solid carbohydrates. An increase in the magnitude of the first order reaction rate constants as the reaction proceeds, which was noted in the early part of the run at 240° C., probably indicates that a similar process is involved even above the melting point. The increased surface here may be due to bubble formation.

Since no attempt was made to isolate and identify the solid products of this reaction, no comprehensive discussion of the organic chemistry involved is possible. Some interesting comparisons can be considered, however, based on the work of others. Pictet and his associates (5-9) have heated a number of carbohydrates under reduced pressure and in nearly all cases showed that glucosans and other anhydrides could be formed.

The formation of a glucosan from cellobiose requires the elimination of one molecule of water from the carbohydrate molecule. Examination of Figs. 3 and 4 shows no sign of a discontinuity in the reaction after the removal of 5% of water, and this would seem to preclude the possibility of glucosan formation unless the cellobiose molecule contained a molecule of water of hydration attached with a bond strength similar in magnitude to water of constitution. Such a situation is very unlikely and indeed a combustion analysis showed the carbon-to-hydrogen ratio to be the theoretical for $C_{12}H_{22}O_{11}$. This must mean that the anhydride formed when cellobiose is heated under the conditions used here involves the loss of two moles of water per mole of cellobiose. The production of 10.5% of water, which is required for this, is in fair agreement with the 10% found here by extrapolation, due allowance being made for the quantities of solid lost by distillation. The loss of more than one molecule of water with the formation of a polymer has been reported by Reilly (13) during the pyrolysis of sucrose, and the similar behavior of cellobiose is not unreasonable.

Maltose

Since maltose differs from cellobiose only in the type of linkage between the two glucose molecules, it might reasonably be assumed that their behavior on thermal decomposition would be similar. This was not found to be the case, however, as the data will show.

The maltose used was a product of the Pfanstiel Chemical Co. labelled "Pure monohydrate". It was soon observed that maltose decomposed much more easily than cellobiose, and the runs were, of necessity, conducted at much lower temperatures. The results obtained at the various temperatures are shown in Table II. Owing to the rapid loss of the water of hydration and the low melting point of maltose monohydrate, a good deal of foaming occurred in the reaction vessel, and it was necessary to use samples sufficiently small to avoid the formation of isolated volumes of foam that would withhold a portion of the reaction products.

TABLE II
VARIATION IN THE DECOMPOSITION WITH TEMPERATURE

Temp., °C.	Time, hr.	Volatile products produced		
		H ₂ O, %	CO ₂ , cc./gm. at N.T.P.	CO, cc./gm. at N.T.P.
150	2	2.60	0.224	—
	5	5.48	0.505	—
	21	11.1	1.31	—
	28	12.6	1.57	—
	45	14.7	2.04	0.252
160	0.5	1.37	0.226	—
	1.3	4.30	0.381	0.018
	3.0	7.15	0.656	0.042
	5.0	9.48	0.930	0.067
	8.0	12.1	1.32	0.092
	11.5	14.3	1.61	0.118
	15.5	15.8	2.16	0.160
	18.5	16.5	2.38	0.219
	24.0	17.6	2.62	0.254
180	0.33	5.55	0.508	—
	1.00	9.95	1.24	0.100
	2.00	13.6	1.95	0.190
	4.00	17.0	2.81	0.327
	6.00	18.5	3.40	0.443
190	0.25	7.58	0.76	—
	0.75	14.0	1.94	0.183
	1.25	17.1	2.76	0.343
	2.25	19.3	3.59	0.561
240*	100	37.9	26.0	11.2

* This may be taken to represent approximately complete reaction.

As with cellobiose, a white, water soluble crystalline compound and a clear syrup distilled from the reactor in small quantities. The solid reaction product remaining in the reactor was easily soluble in water after 16% of water had been removed. In this respect it differed considerably from cellobiose, which became difficultly soluble in water at a much lower degree of dehydration.

The loss of the molecule of water of hydration took place much more rapidly than the remaining decomposition, and the results in Table II and those shown in Fig. 6 are reported in terms of anhydrous maltose.

An activation energy of 35 kcal. was found. This value is somewhat lower than the lowest value obtained with cellobiose. However, in contrast with the values obtained for cellobiose, it was fairly constant throughout the experimental decomposition range, and no evidence of a second reaction of different activation energy could be found.

Product vs. time curves for maltose gave no indication of sigmoid shape. As noted earlier, however, owing to foaming in the early stages of the reaction the solid present would be in an extremely finely divided state and this could

mask the presence of an induction period. First order reaction rate constants calculated on the assumption that 100 hr. at 240° C. represents complete reaction showed no increase in magnitude as the reaction proceeds, but rather tended to fall off. This is contrary to the behavior of normal solid decompositions and indicates the decomposition either of a liquid or an extremely finely divided solid.

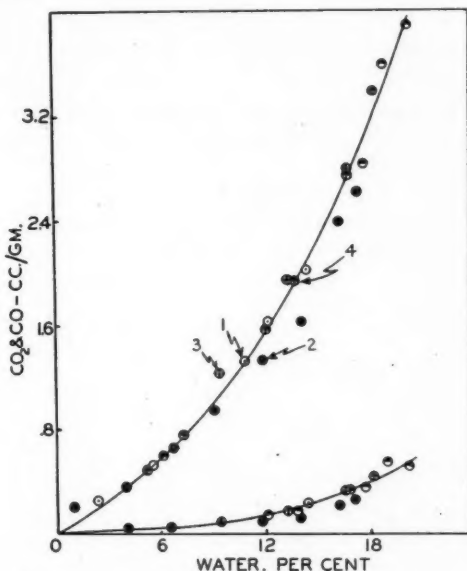


FIG. 6. The effect of temperature on the product ratio in the thermal decomposition of maltose. Curves 1, 2, 3, and 4 represent results obtained at 150°, 160°, 180°, and 190° C. Upper graph represents carbon dioxide; lower graph, carbon monoxide.

With cellobiose the reaction eventually reached a stage where the amount of carbon dioxide and carbon monoxide produced bore a linear relation to the amount of water formed in the decomposition. An examination of Fig. 6 shows that this condition never obtained with maltose. It is also apparent from this graph that, within experimental error, the ratio of the products formed is not a function of temperature. The decomposition appears to be a single reaction, with no indication of anhydride or polymer formation. The water solubility of the solid product and the constancy of the activation energy support this contention.

Pictet and Marfort (7) considered that the solid formed on heating maltose at 160° C. and a pressure of about 15 mm. was the anhydride maltosan, since analysis indicated a formula of $C_{12}H_{20}O_{10}$. However, they do note a number of peculiarities shown by this material that distinguished it from other sugar anhydrides. The results of the present work would suggest that Pictet was dealing not with maltosan but rather with a lower decomposition product of maltose.

The striking difference in the behavior of maltose and cellobiose is surprising and must be attributed to the different molecular geometry caused by the α -glucosidic linkage, which does not allow either the formation of anhydrides in single molecules or condensation between several molecules to give polymers under the conditions of these experiments.

Dextrose

The behavior of dextrose, which may be considered a monomer of maltose and cellobiose, is described below.

The dextrose used was Merck's C.P. anhydrous. It was examined over the temperature range of 170° to 210° C., and the results are shown in Table III.

TABLE III
VARIATION IN THE DECOMPOSITION WITH TEMPERATURE

Temp., °C.	Time, hr.	Volatile products produced		
		H ₂ O, %	CO ₂ , cc./gm. at N.T.P.	CO, cc./gm. at N.T.P.
170	2	7.00	0.129	
	4	9.33	0.266	
	7	10.69	0.419	
	25.5	12.78	0.668	
	32.5	12.88	0.773	
	49.5	13.17	0.950	
180	1	7.13	0.112	
	3	9.82	0.298	0.130
	5	11.61	0.464	0.209
	22	13.91	1.06	0.300
	46	14.50	1.64	0.437
190	0.3	5.67	0.090	
	1.3	10.95	0.352	0.057
	2.0	11.75	0.485	0.128
	2.8	12.22	0.529	0.144
	4.0	13.19	0.801	0.221
	7.0	13.91	1.06	0.289
	24	15.20	2.08	0.502
200	0.5	8.55	0.103	
	1.5	12.51	0.535	0.096
	3.5	13.86	1.03	0.184
	8.5	14.88	1.87	0.400
210	0.3	10.00	0.367	
	1.0	12.67	0.923	0.159
	4.5	14.55	2.11	0.279
	21.5	17.10	4.83	1.08

When the data from Table III are presented graphically as in Fig. 7, it is evident that the reaction is complex. The first step, the loss of 5% of water, is obviously much faster than the subsequent steps. Indeed, Table III shows that over the temperature range examined no data are available for

water production in quantities of less than 5%. Since this amount corresponds exactly to one mole of water for two moles of dextrose, the first step in the reaction must be a condensation dimerization.



Further indication of this is given if one follows the reaction at temperatures below the melting point of the dextrose. At 130° C., for example, about 120 hr. are required for the loss of 5% of water, and at this point the buff colored solid melts to a viscous liquid. This is possibly due to the formation of more than one isomeric disaccharide, with the consequently low mixed melting point. The product appeared to be the same whether formed at 130° or 215° C.

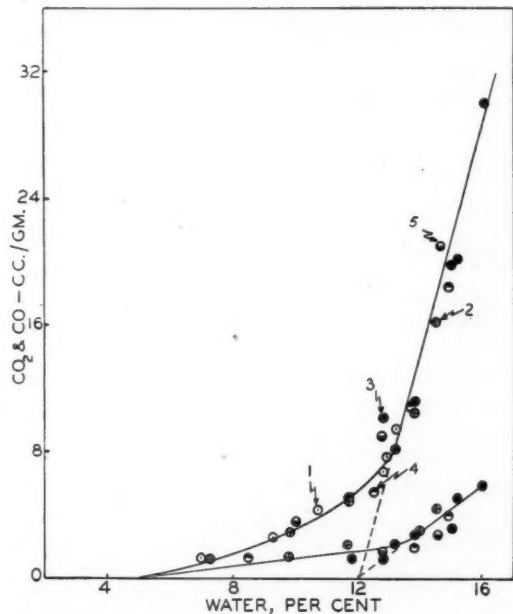


FIG. 7. Product ratio at various temperatures. Curves 1, 2, 3, 4, and 5 represent results obtained with dextrose at 170°, 180°, 190°, 200°, and 210° C. Upper graph represents carbon dioxide; lower graph, carbon monoxide.

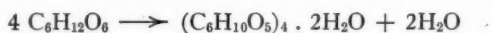
When cooled, the material was an amber colored glass that dissolved in water easily and precipitated as a tar if the water solution was added to a large excess of alcohol. No success was obtained in attempts to crystallize it from water plus alcohol in various ratios or from pyridine. The aqueous solution reduced Fehling solution strongly and fermented readily with yeast. Oxidation with alkaline iodine by the method of Hinton and Macara (3)

indicated that one aldehyde group of the original glucose had been lost in the condensation. The aldehyde content increased on continued heating with water. This suggested some hydrolysis.

The product acetylated readily with acetic anhydride and sodium acetate. No success was obtained, however, in attempts to crystallize the acetyl compound from methanol in the usual way.

Pictet and Vogel (9) have shown that a good yield of glucosan is obtained by heating anhydrous glucose at 150° C. and 15 mm. pressure. These conditions are not greatly different from those used here and a similar reaction might be expected. If this is the case the glucosan must be formed from the dimer by the loss of a second molecule of water.

A second possible explanation of the 5% water loss is suggested by the work of Pictet and Pictet (8) who showed that glucose heated to 180° C. in the presence of zinc chloride dehydrated and polymerized to form a dihydrate of a glucosan tetramer, which was extremely stable.



While no catalyst was used in the present work, the pressure at which the reaction was maintained was much less, 10^{-5} mm. compared to 15 mm. for Pictet's work, and this might produce a similar effect. It would be expected, however, that in a molecule of this type the water of hydration would be less tightly held than water of constitution, and further degradation should cause a second loss of precisely 5% of water, before water of constitution or carbon dioxide would be evolved. Since this did not occur, the mechanism of dimerization appears to be favored. Further, the joining of two molecules of dextrose by a 1-6 glucosidic linkage to give gentiobiose has been described (1), and while no gentiobiose was identified in the solid product, the subsequent behavior of the reaction strongly suggests the formation of disaccharides.

The behavior of the reaction following the first step resembles the decomposition of cellobiose. If the data are plotted on a much larger scale, there is a slight decrease in the amount of carbon dioxide produced for a given quantity of water, as the reaction temperature is increased. The spread is not great, however, and does not show in the present plot. This indicates that while the dehydration and the production of oxides of carbon are probably the result of separate reactions, as was the case with the cellobiose decomposition, the activation energies for the two reactions are similar and they cannot be separated by changing the temperature at which the decomposition is carried out.

After 12% of water is lost, the same linear relation between the amounts of carbon dioxide and water produced that was found with cellobiose appears. The extrapolated value of the water is again in excess of that required for the formation of glucosan, and the only explanation that appears to be tenable involves the formation of anhydrides with a water content lower than that of

glucosans. The similarity of the decomposition of this anhydride to that of starch suggests the probability of its existing as a polymer, and the molecular weight found by Pictet supports this. The extrapolated value of 12% of water indicates that approximately 60% of the dimer may decompose to give glucosan and the remainder loses two molecules of water. Loss of a single molecule may be favored at lower temperatures, since Pictet obtained a 92% yield of glucosan from glucose at 145° C., although the present work gives no indication of this.

The activation energy for the reaction was found to be 29 kcal. This was constant over the range of 6 to 13% of water formed by the decomposition. The long times required for the reaction at the lower temperatures prevented the extension of this to higher percentages of water, which would have been desirable in view of the closeness of the upper limit to the critical value of 12% found by extrapolation. In contrast to the behavior of cellobiose there was no indication of a break in the activation energy vs. percentage water plot, to give definite evidence of the splitting off of the second and third water molecules by separate reactions. The general behavior of the dimer is intermediate between that of maltose and of cellobiose, and the dimer may be an isomer of them.

The similar carbon dioxide - water ratio found in the decomposition products of the polymers formed from the anhydrides of cellobiose and dextrose with starch is somewhat surprising, since the starch polymer consists of $C_6H_{10}O_5$ units while the sugars form lower anhydrides. This decomposition, however, probably depends on internal rearrangements of the molecule after dehydration to give carboxyl groups from which carbon dioxide may be formed, and this, within reasonable limits, may not depend greatly on the degree of dehydration.

Potato Starch

As pointed out previously the dextrinization of starch without catalysts proceeds much faster at reduced pressure than it does if the starch is exposed to air at the same temperature. This appears to preclude the possibility that dextrinization is a partial oxidation, as is sometimes suggested (4, p. 245), and the fact that water and oxides of carbon are formed indicates that the process is a thermal decomposition. The data obtained when the degradation of dry potato starch was followed over the temperature range 180° to 210° C. are presented in Table IV.

The starch used in the work was a high grade product obtained from the F. W. Pirie Co.; it contained 15.5% of water prior to dehydration.

An examination of Fig. 8 shows that the ratio of the decomposition products is independent of temperature over the range examined. The ratio of carbon dioxide to water appears to be identical with that obtained with dextrose and cellobiose; the relation is linear until about 10% of water is evolved. In view of the behavior of the sugars it is significant that no dehydration as a separate reaction takes place with potato starch. A second point of interest

TABLE IV
VARIATION IN THE DECOMPOSITION WITH TEMPERATURE

Temp., °C.	Time, hr.	Volatile products		
		H ₂ O, %	CO ₂ , cc./gm. at N.T.P.	CO, cc./gm. at N.T.P.
180	1	0.18	0.042	0.048
	4	0.28	0.072	0.153
	9.5	0.41	0.122	0.289
	26.5	0.75	0.292	0.502
	50.5	1.16	0.778	0.683
	74.5	1.56	1.03	0.826
	98.5	1.92	1.24	0.945
190	3	0.26	0.220	0.185
	23	1.13	0.727	0.596
	71	2.38	1.68	1.05
	95	3.07	2.18	1.30
	119	3.75	2.61	1.49
200	1		0.031	0.110
	3	0.19	0.135	0.280
	6	0.59	0.322	0.436
	23	2.09	1.23	0.860
	29	2.48	1.45	0.955
	46	3.80	2.33	1.29
	70	6.03	3.90	1.78
	105	8.40	5.60	2.33
	128	10.2	7.00	2.79
	149	12.1	8.25	3.07
210	1	0.24	0.116	0.172
	3	0.88	0.486	0.418
	22	6.14	4.12	1.66
	46	12.7	8.85	3.14
	70	16.7	11.7	4.16
	94	19.1	13.8	4.92
	118	20.9	15.3	5.55
	142	22.1	16.5	6.06
	8 days	26.6	22.1	9.30

is the high carbon monoxide - carbon dioxide ratio, which initially exceeds the value obtained with the sugars by a factor of 4. This ratio does not remain constant but falls off, after about 1% of water has been lost, to a value of approximately 1 : 3. The dextrin formed was a faint yellow after the removal of 0.25% of water and the color deepened to a dark brown as the reaction proceeded. The water solubility increased enormously in the early stages of the decomposition and the viscosity of the dispersion decreased in about the same proportion.

Although the ratio of carbon dioxide to water found with cellobiose and dextrose indicates a close similarity between the polymers formed from these sugars and starch, the unit is considerably different, as shown by the relatively large amounts of carbon monoxide that are formed from the starch. It is quite probable that rearrangements take place after the removal of water,

and the formation of larger numbers of carbonyl groups from which the carbon monoxide may be derived relative to carbon dioxide producing groups is possibly due to the larger molecular size of the starch.

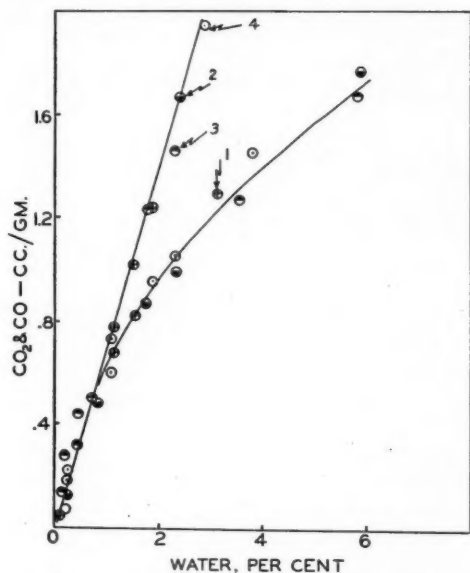


FIG. 8. Product ratio for anhydrous potato starch at various temperatures. Curves 1, 2, 3, and 4 represent data obtained at 180°, 190°, 200°, and 210° C. Upper graph represents carbon dioxide; lower graph, carbon monoxide.

The activation energy for the reaction was found to be fairly constant at 29 kcal. over the range of 1 to 4% of water given off, with no indication of side reactions.

Since all the temperatures used in this work are below the fusion point of starch, it is of interest to consider briefly the theory of Prout and Tompkins on the thermal decomposition of solids. The granules of starch are very small (in this case the average diameter would approximate 30 μ), and the percentage increase in surface area caused by fissures that may be formed during the decomposition would not be sufficiently large to show an appreciable induction period. A plot of any of the products produced vs. time does not give a sigmoid curve but resembles the curve obtained for a normal first order reaction. However, on the assumption that eight days at 210° C. represents complete reaction, first order reaction rate constants have been calculated for the 200° and 210° C. runs based on the amount of carbon dioxide produced and these are shown in Table V. At 200° C., the values increase continuously during the time the reaction was followed; at 210° C., where the reaction was followed to completion, the rate constants increase to a maximum and then fall off. This is clearly indicative of an autocatalytic period followed

TABLE V
RATE CONSTANTS BASED ON CARBON DIOXIDE PRODUCED

Temp., °C.	Time, hr.	k , hr. ⁻¹	Temp., °C.	Time, hr.	k , hr. ⁻¹
200	1	1.4×10^{-3}	210	1	4.6×10^{-3}
	3			3	
	6			22	
	23			46	
	29			70	
	46			94	
	70			118	
	105			142	
	128				
	149				

by a decay after the maximum rate has been attained. While the period of acceleration of the reaction might be due to the formation of small quantities of organic acids from the decomposition which could cause catalysis, the falling-off in the rate would be difficult to explain on this basis. It seems more probable that the acceleration and decay are due to changes in the rate of new surface formation by cracks and fissures in the granules. In support of this, the gradual fading of the bright pattern, observed when starch is examined microscopically between crossed Nicols, during the course of the reaction is indicative of structural changes within the granule.

The ratio of carbon dioxide to water obtained during the thermal decompositions of four similar carbohydrates is shown graphically in Fig. 9. The similarity in the behavior of dextrose, cellobiose, and starch is evident, while the behavior of maltose is definitely anomalous.

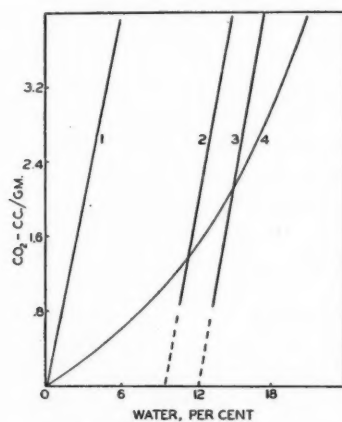


FIG. 9. Carbon dioxide vs. water in the thermal decomposition products of several carbohydrates. Curves 1, 2, 3, and 4 represent respectively data obtained from potato starch, cellobiose, dextrose, and maltose.

References

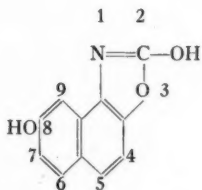
1. BERLIN, H. J. Am. Chem. Soc. 48 : 2627. 1926.
2. GARNER, W. E. Trans. Faraday Soc. 34 : 940. 1938.
3. HINTON, C. L. and MACARA, T. Analyst, 49 : 2. 1924.
4. KERR, R. W., *Editor*. Chemistry and industry of starch. Academic Press, Inc., New York. 1944.
5. PICTET, A. and ANDRIANOFF, N. Helv. Chim. Acta, 7 : 703. 1924.
6. PICTET, A. and EGAN, M. M. Helv. Chim. Acta, 7 : 295. 1924.
7. PICTET, A. and MARFORT, A. Helv. Chim. Acta, 6 : 129. 1923.
8. PICTET, A. and PICTET, J. Helv. Chim. Acta, 4 : 788. 1921.
9. PICTET, A. and VOGEL, H. Helv. Chim. Acta, 9 : 806. 1926.
10. PROUT, E. G. and TOMPKINS, F. C. Trans. Faraday Soc. 40 : 488. 1944.
11. PROUT, E. G. and TOMPKINS, F. C. Trans. Faraday Soc. 42 : 468. 1946.
12. PUDDINGTON, I. E. Ind. Eng. Chem., Anal. Ed. 16 : 592. 1944.
13. REILLY, J. J. Soc. Chem. Ind. 40 : 249 T. 1921.

NOTES

A Note on the Preparation of Benzoxazolone and of 2,8-Dihydroxynaphth[1,2]oxazole

Some time ago we required considerable amounts of benzoxazolone. As this has frequently been prepared by inconvenient methods, we report here an excellent one suggested by Sandmeyer (4). He mentions that benzoxazolone can be prepared by heating *o*-aminophenol hydrochloride with urea, but gives no details.

We also had occasion to prepare 2,8-dihydroxynaphth[1,2]oxazole, the synthesis of which, using phosgene, has been described in the patent literature (3). It, too, may be obtained by Sandmeyer's method from the hydrochloride of 1-amino-2,7-dihydroxynaphthalene. The latter was prepared from 2,7-dihydroxynaphthalene over its 1-nitroso derivative, essentially according to Clausius (1).



Formula of 2,8-dihydroxynaphth[1,2]oxazole to show the numbering of positions in naphth[1,2]oxazoles.

Experimental

Benzoxazolone.—A mixture of *o*-aminophenol (Eastman Kodak, 'practical'; 110 gm.), urea (200 gm.) and hydrochloric acid (125 cc.) was heated, in a beaker with occasional stirring, to 140° C., held at 140° C. for half an hour, then at 150° to 160° C. for half an hour. Water (500 cc.) and hydrochloric acid (25 cc.) were added to the hot mixture. After cooling the product was filtered off, washed with water, dried, and distilled, b.p. 184° to 185° C. (8 mm.); m.p. 138.5° to 139°; 138° to 139° C. has been recorded for the latter (2). Yield, 103 gm. (76%).

1-Nitroso-2,7-dihydroxynaphthalene.—2,7-Dihydroxynaphthalene (50 gm.) was dissolved in hot water (1 liter) and cooled quickly; sodium nitrite (23 gm.), water (500 cc.), and chipped ice (1 kgm.) were then added. The mixture was stirred at 0° C. while sulphuric acid (10 cc.) in water (250 cc.) was dropped in over two hours. After stirring another hour, any excess nitrous acid was removed by adding ammonium sulphamate. The product was filtered off and washed with water (2 liters). It was not pressed down on the filter.

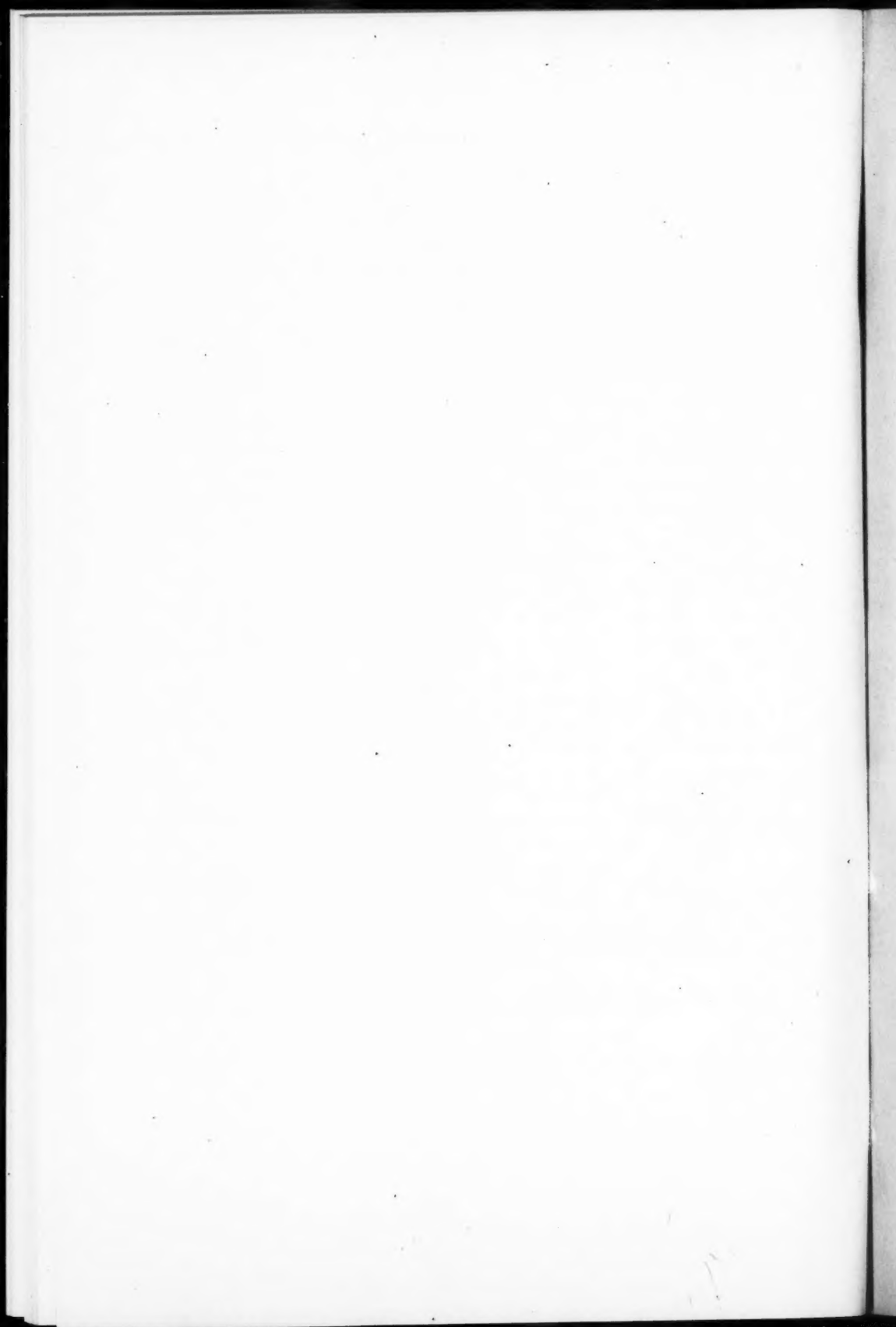
Hydrochloride of 1-Amino-2,7-dihydroxynaphthalene.—The damp nitroso-derivative was slurried with water (800 cc.) and stannous chloride solution (460 cc.) (prepared by dissolving 105 gm. tin in 600 cc. hydrochloric acid) was added. The mixture was heated to boiling and filtered. The product was precipitated from the clear yellow filtrate by adding hydrochloric acid (1.5 liters) and cooling; it was filtered, washed with dilute (1 : 1) hydrochloric acid (150 cc.) and pressed as dry as possible.

2,8-Dihydroxynaphth[1,2]oxazole.—The amine hydrochloride was heated with urea (100 gm.) in an oil bath. After the temperature reached 110° C. it was allowed to rise slowly over one hour to 140° C., and kept at this temperature for one hour. The progress of the reaction was followed by observing the diminution in the color produced when a sample was treated with caustic soda solution. The cooled mass was ground up and washed with water. It was then dissolved in water (600 cc.) containing potassium hydroxide (30 gm.), filtered with charcoal (20 gm.), and the crude product precipitated by acidifying the filtrate. It was purified by dissolving in a hot mixture of pure pyridine (200 cc.) and alcohol (200 cc.), adding hot water (350 cc.), heating for 20 min. with charcoal (50 gm.), filtering, adding hot water (1 liter) to the filtrate, and allowing the product to crystallize slowly. It forms light-brown prisms (37 gm.) (60% over-all yield), decomposing at a high temperature. Calc. for $C_{11}H_7O_3N$: C, 65.67; H, 3.51; N, 6.96%. Found: C, 65.8; H, 4.00; N, 6.78%.

1. CLAUSIUS, A. Ber. 23 : 517. 1890.
2. GRAEBE, C. and ROSTOVZEFF, S. Ber. 35 : 2747. 1902.
3. I. G. FARBENIND. AKT.-GES. Fr. Patent 789,725. Nov. 5, 1935. Chem. Abstracts, 30 : 3252. 1936.
4. SANDMEYER, T. Ber. 19 : 2650. 1886.

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